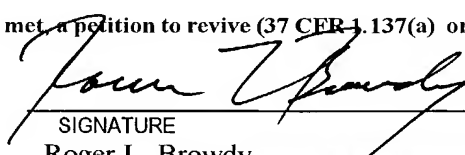


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JC20 Rec'd PCT/PTO 25 FEB 2002

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER KAIHO=3
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 10/069282
INTERNATIONAL APPLICATION NO. PCT/JP00/05636	INTERNATIONAL FILING DATE 23 August 2000	PRIORITY CLAIMED 23 August 1999
TITLE OF INVENTION ANTIANDROGENIC AGENTS		
APPLICANT(S) FOR DO/EO/US Shin-ichi KAIHO et al.		
<p>Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:</p> <ol style="list-style-type: none"> <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371 <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1) <input checked="" type="checkbox"/> The US has been elected in a Demand by the expiration of 19 months from the priority date (PCT Article 31). <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) <ol style="list-style-type: none"> <input type="checkbox"/> is attached hereto (required only if not transmitted by the International Bureau) <input checked="" type="checkbox"/> has been communicated by the International Bureau <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). <input checked="" type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)) <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) <ol style="list-style-type: none"> <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau) <input type="checkbox"/> have been communicated by the International Bureau <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired <input checked="" type="checkbox"/> have not been made and will not be made. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)) <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)). <p>Items 11. to 16. below concern document(s) or information included:</p> <ol style="list-style-type: none"> <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98 <input type="checkbox"/> An Assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included <input type="checkbox"/> A FIRST preliminary amendment <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment <input type="checkbox"/> A substitute specification <input type="checkbox"/> A change of power of attorney and/or address letter <input checked="" type="checkbox"/> Other items or information: <ul style="list-style-type: none"> <input checked="" type="checkbox"/> Courtesy copy of the first page of the International Publication (WO 01/14406). <input checked="" type="checkbox"/> Courtesy copy of the International Preliminary Examination Report. There were no annexes. <input checked="" type="checkbox"/> Courtesy Copy of the International Search Report <input checked="" type="checkbox"/> Application Data Sheet <p><input checked="" type="checkbox"/> The application is (or will be) assigned to: CHUGAI SEIYAKU KABUSHIKI KAISHA, whose address is 5-1 Ukima 5-chome, Kita-ku, Tokyo 115-8543 Japan.</p>		

U.S. APPLICATION NO. (If known, see 37 CFR 1.5)		International Application No		JC13 Rec'd PCT/PTO 25 FEB 2002	
10/069282		PCT/JP00/05636		KAIHO=3	
17. [xx] The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492 (a)(1) –(5): Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO. \$1040.00 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$890.00 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO.\$740.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$710.00 International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4)... .. \$100.00 ENTER APPROPRIATE BASIC FEE AMOUNT =				CALCULATIONS PTO USE ONLY	
Surcharge of \$130.00 for furnishing the oath or declaration later than [] 20 [] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				\$	890.00
Claims as Originally Presented		Number Filed	Number Extra	Rate	
Total Claims		28 - 20	08	X \$18.00	\$ 144.00
Independent Claims		2 - 3		X \$84.00	\$
Multiple Dependent Claims (if applicable)				+\$280.00	\$ 280.00
TOTAL OF ABOVE CALCULATIONS =				\$1,314.00	
Claims After Post Filing Prel Amend		Number Filed	Number Extra	Rate	
Total Claims		- 20		X \$18.00	\$
Independent Claims		- 3		X \$84.00	\$
TOTAL OF ABOVE CALCULATIONS =				\$1,314.00	
Reduction of ½ for filing by small entity, if applicable Applicant claims small entity status. See 37 CFR 1.27				\$	
SUBTOTAL =				\$1,314.00	
Processing fee of \$130.00 for furnishing the English translation later than [] 20 [] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				\$	
TOTAL NATIONAL FEE =				\$1,314.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property +				\$	
TOTAL FEES ENCLOSED =				\$1,314.00	
				Amount to be:	\$
				refunded	
				charged	\$
a. [] A check in the amount of \$_____ to cover the above fees is enclosed					
b. [X] Credit Card Payment Form (PTO-2038), authorizing payment in the amount of \$ 1,314.00, is attached.					
c. [] Please charge my Deposit Account No 02-4035 in the amount of \$_____ to cover the above fees A duplicate copy of this sheet is enclosed.					
d. [XX] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 02-4035. A duplicate copy of this sheet is enclosed					
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.					
SEND ALL CORRESPONDENCE TO					
BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, N.W., SUITE 300 WASHINGTON, D.C. 20001 TEL: (202) 628-5197 FAX: (202) 737-3528 Date of this submission: MONDAY, February 25, 2002					
				SIGNATURE  Roger L. Browdy NAME 25,618 REGISTRATION NUMBER	
Form PTO-1390 (as slightly revised by Browdy and Neimark)					

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Rec'd PCT/PTO 25 FEB 2002

SPECIFICATION

ANTIANDROGENIC AGENTS

TECHNICAL FIELD

5 This invention relates to androstane derivatives
having various substituents in 7- or 11-position,
substances that act as antagonist against but not as
agonist for the androgen receptor, and pharmaceuticals that
contain said androstane derivatives and said substances.

10

BACKGROUND ART

 It has become known to date that prostate cancer,
prostatomegaly, male pattern alopecia, sexual prematurity,
acne vulgaris, seborrhea and hirsutism are closely
15 associated with the male hormone, androgen. For example,
it is known that prostate cancer and prostatomegaly are
rare in castrated men and patients with gonad dysfunction.

 Already used antiandrogenic agents, or agonists for
the androgen receptor, include, for example, cyproterone
20 acetate, chlormadinone acetate, flutamide and bicaltamide.
Cyproterone acetate is known to suppress the progress of
acne and the onset of baldness in the teens. Cyproterone
acetate is also used in women for treatment of
masculinization and alopecia. Flutamide and bicaltamide
25 are used as therapeutics for prostatomegaly.

 These antiandrogenic agents have exhibited marked
efficacy in many cases including drug therapy of prostate
cancer and comprise an important part of the effective

therapeutics. However, one of the problems with these antiandrogenic agents is that even if they exhibit marked efficacy, recurrence is common in almost all cases after the lapse of two to five years; in other words, they are known to induce androgen tolerance.

It was recently reported that hydroxyflutamide, the active essence of flutamide, elevated the transcriptional activity of the androgen receptor at a concentration of 10 mol/L. Plasma levels of hydroxyflutamide in prostate cancer patients under flutamide treatment are several mol/L which, according to the report, is the level at which the agonist action is manifested (see J. Biol. Chem., vol. 270, 19998-20003, 1995). It was also reported that a two-week continuous administration of cyproterone acetate and chlormadinone acetate to castrated rats increased the prostate weight (Folia endocrinol., vol. 66, 597-606, 1990). As for flutamide and bicartamide, cases of side effects such as hepatotoxicity have also been reported.

Speaking of the so-called pure antagonists which are substances that act as antagonist against but not as agonist for a nuclear receptor, namely, substances that can completely inhibit the action of the receptor, they have been known for the estrogen receptor (see, for example, WO98/25916, European Patent Publication No. 0138504, USP 4,659,516 and Cancer Res., 1991, 51, 3867). The molecular structures of the hormone-binding domains of nuclear receptors are being unravelled by X-ray crystallography and

the like for RXR (retinoid-X receptor), RAR (retinoic acid receptor) and the like (see, for example, Nature, vol. 375, 377-382, 1995).

5 WO97/49709 discloses androgen receptor modifiers that are nonsteroidal four-ring compounds.

Steroid compounds having an aminocarbonylalkyl group in 7-position or an aminocarbonylalkynyl group in 17-position are known by being described in WO91/00732. These are androgen synthesis inhibitors and/or substances that
 10 act as antanosit against the androgen receptor and steroid compounds are disclosed that have a freely selectable double bond in 1(2) position, 4(5) position, 6(7) position, 9(10) position and/or 11(12) position in the general formula and the only specific compounds that are disclosed
 15 have a double bond in 4(5) position. One of the compounds that are mentioned as the most preferred is EM-101 which is a steroid compound having a 10-(N-butyl-N-methylaminocarbonyl)decyl group in 7 α -position and a hydroxyl group in 17 β -position. However, these compounds
 20 have problems such as inadequate antagonist action against the androgen receptor, strong toxicity, etc.

As a steroid compound having an aromatic ring or an alkyloxy group in 11-position, RU486 is described in WO95/17192 and known as an agent for dealing with multi-
 25 drug tolerance.

DISCLOSURE OF INVENTION

An object of the this invention is to provide

SECRET

androstane derivatives having various substituents in 7- or 11-position, pharmaceutically acceptable salts thereof, or prodrugs of the derivatives or their salts.

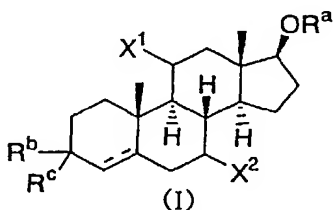
Another object of this invention is to provide
5 substances that act as antagonist against but not as agonist for the androgen receptor, pharmaceutically acceptable salts thereof, or prodrugs of the substances or their salts.

Still another object of this invention is to provide
10 pharmaceuticals that contain said androstane derivatives and pharmaceuticals that contain said substances.

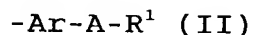
With a view to attaining these objects, the present inventor hypothesized that one of the causes of side effects, such as androgen tolerance and the increase in
15 prostate weight, that are developed by heretofore known antagonists against the androgen receptor is the proliferation of androgen-responsive cells (e.g. prostate cells) due to the agonist action possessed by said antagonists, and anticipated that finding a pure antagonist
20 against the androgen receptor, namely, an antagonist that does not act as agonist for the androgen receptor, would lead to the finding of antiandrogenic agents that do not show any side effects such as the development of androgen tolerance and hepatotoxicity after prolonged administration;
25 the inventor then undertook the designing of said antagonist. To begin with, the androgen receptor was modelled from existing nuclear receptors such as RXR and RAR by the homology technique using software packages such

as Homology (from MSI) and Look (from MAG). Second, it was found that if a pure antagonist against the androgen receptor was designed by using testosterone and/or dihydrotestosterone as a ligand and, with the resulting model of a complex between said ligand and the androgen receptor being utilized, by introducing into suitable positions those side chains which had suitable lengths and functional groups to form the interaction with the receptor, substances or compounds could be designed that could be anticipated to act as pure antagonist against the androgen receptor and/or antiandrogenic agents that had lesser side effects such as lower hepatotoxicity; the present invention has been accomplished on the basis of this finding.

According to a first aspect of this invention, there
15 are provided compounds represented by the general formula
(I), pharmaceutically acceptable salts thereof, or prodrugs
of the compounds or their salts:



[wherein X^1 and X^2 represent independently a hydrogen atom
20 or a group represented by the general formula (II)]



R^a represents a hydrogen atom or a protective group of a hydroxyl group, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound,

represent an optionally protected $-(C=O)-$, and the dashed line in combination with the solid line represents the formation of a single bond or a double bond;

in addition, Ar represents a single bond or an aromatic hydrocarbon group, A represents a methylene group or -O-, R¹ represents an optionally substituted alkyl group, an optionally substituted alkenyl group or an optionally substituted alkynyl group;

provided that X^1 and X^2 are not a hydrogen atom at the
10 same time].

According to a second aspect of this invention, there are provided substances that act as antagonist against but not as agonist for the androgen receptor, pharmaceutically acceptable salts thereof, or prodrugs of the substances or
15 their salts.

According to a third aspect of this invention, there are provided pharmaceuticals that contain compounds represented by the general formula (I), as well as pharmaceuticals that contain substances that act as antagonist against but not as agonist for the androgen receptor.

BEST MODE FOR CARRYING OUT THE INVENTION

In this specification, straight-chained or branched
25 alkyl groups having 1 - 3 carbon atoms include methyl group,
ethyl group, n-propyl group and i-propyl group.

Straight-chained or branched alkyl groups having 1 - 6 carbon atoms include, for example, methyl group, ethyl

group, n-propyl group, i-propyl group, n-butyl group, s-butyl group, i-butyl group, t-butyl group, n-pentyl group, 3-methylbutyl group, 2-methylbutyl group, 1-methylbutyl group, 1-ethylpropyl group and n-hexyl group.

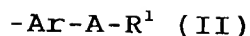
5 In this specification, ω position means the terminal position of a divalent group which is other than 1-position. For example, in hexane-1,6-diyl group, ω position is 6-position.

10 In this specification, the single bond means that the group of interest does not exist but that the groups adjacent both sides of said group directly form a single bond. For example, to say Ar is a single bond in the group represented by the general formula (II) shows that 7-position and/or 11-position of the steroid ring in the
15 compound represented by the general formula (I) and A directly form a single bond.

20 In this specification, to say that the dashed line in combination with the solid line represents the formation of a single bond or a double bond means, for example, that the bond between 4-position and 5-position of the steroid ring denoted by the dashed line is a single bond or a double
25 bond. This is also true with compound (2) in process A to be described later and it is meant that the bond between 5-position and 6-position of the steroid ring denoted by the dashed line is a single bond or a double bond.

 In the definition of the compounds represented by the general formula (I), X^1 and X^2 represent independently a hydrogen atom or a group represented by the general formula

(II)



(wherein, in addition, Ar represents a single bond or an aromatic hydrocarbon group, A represents a methylene group or -O-, R¹ represents an optionally substituted alkyl group, an optionally substituted alkenyl group or an optionally substituted alkynyl group); preferred are the case where X¹ is -Ar-A-R¹ (wherein Ar, A and R¹ have the same meanings as defined above) and X² is a hydrogen atom, and the case where X¹ is a hydrogen atom and X² is -Ar-A-R¹ (wherein Ar, A and R¹ have the same meanings as defined above). Further preferred are compounds in which the steric configuration of X¹ in 11-position of the steroid ring is β configuration and those in which the steric configuration of X² in 7-position is α configuration. Note that X¹ and X² are not a hydrogen atom at the same time.

While R^a represents a hydrogen atom or a protective group of a hydroxyl group, a hydrogen atom is preferred. Protective groups of a hydroxyl group include acyl groups such as formyl group, acetyl group, propionyl group, butyryl group, isobutyryl group, valeryl group, isovaleryl group, pivaloyl group, caproyl group, trifluoroacetyl group and benzoyl group, alkoxycarbonyl groups such as methoxycarbonyl group, ethoxycarbonyl group, propoxycarbonyl group, isopropoxycarbonyl group, allyloxycarbonyl group, benzyloxycarbonyl group and phenoxycarbonyl group, substituted silyl groups such as trimethylsilyl group, triethylsilyl group,

triisopropylsilyl group, dimethylisopropylsilyl group, diethylisopropylsilyl group, dimethyltetylalsilyl group, t-butyl dimethylsilyl group, t-butyl diphenylsilyl group, tribenzylsilyl group, tri-p-xylylsilyl group,

5 triphenylsilyl group, diphenylmethylsilyl group and t-butylmethoxyphenylsilyl group, substituted methyl groups such as methoxymethyl group, methoxyethoxymethyl group, methylthiomethyl group, t-butylthiomethyl group, β -trichloroethyloxymethyl group, trimethylsilylethoxymethyl

10 group, p-methoxybenzyloxymethyl group and p-chlorobenzyloxymethyl group, 2-oxacycloalkyl groups such as tetrahydrofurallyl and tetrahydropyranyll, and aralkyl groups such as benzyl group. Among these, substituted silyl groups such as trimethylsilyl group, triethylsilyl

15 group, triisopropylsilyl group, dimethylisopropylsilyl group, diethylisopropylsilyl group, dimethyltetylalsilyl group, t-butyl dimethylsilyl group, t-butyl diphenylsilyl group, tribenzylsilyl group, tri-p-xylylsilyl group, triphenylsilyl group, diphenylmethylsilyl group and t-

20 butylmethoxyphenylsilyl group, as well as substituted methyl groups such as methoxymethyl group, methoxyethoxymethyl group, methylthiomethyl group, t-butylthiomethyl group, β -trichloroethyloxymethyl group, trimethylsilylethoxymethyl group, p-methoxybenzyloxymethyl

25 group and p-chlorobenzyloxymethyl group are preferred, and t-butyl dimethylsilyl group and methoxymethyl group are particularly preferred.

R^b and R^c , when taken together with the carbon atom in

3-position to which they are bound, represent an optionally protected $-(C=O)-$ and they preferably represent $-(C=O)-$. Examples of protected $-(C=O)-$ include noncyclic acetals or ketals such as dimethoxystyrene, bis(2,2,2-

5 trichloroethyloxy)methylene, dibenzylmethylene, bis(2-nitrobenzyloxy)methylene, bis(acetyloxy)methylene, bis(methylthio)methylene, bis(ethylthio)methylene, bis(propylthio)methylene, bis(butylthio)methylene, bis(phenylthio)methylene, bis(benzylthio)methylene,

10 bis(acetylthio)methylene, trimethylsilyloxymethylthiomethylene, trimethylsilyloxyethylthiomethylene, trimethylsilyloxyphenylthiomethylene, methyloxymethylthiomethylene, methyloxyphenylthiomethylene,

15 methyloxy-2-(methylthio)ethylthiomethylene, bis(methylselenenyl)methylene and bis(phenylselenenyl)methylene, and cyclic acetals or ketals such as 1,3-dioxane, 5,5-dibromo-1,3-dioxane, 5-(2-pyridyl)-1,3-dioxane, 1,3-dioxolane, 4-bromomethyl-1,3-

20 dioxolane, 4-(3-butenyl)-1,3-dioxolane, 4-phenyl-1,3-dioxolane, 4-(2-nitrophenyl)-1,3-dioxolane, 4,5-dimethoxymethyl-1,3-dioxolane, 1,5-dihydro-3H-2,4-benzodioxepin, 1,3-dithian, 1,3-dithiolan, 1,5-dihydro-3H-2,4-benzodithiepin and 1,3-oxathiolan; preferred are 1,3-

25 dioxane, 1,3-dioxolane and 1,3-dithian, etc. and particularly preferred are 1,3-dioxolane, etc.

The dashed line denotes that in combination with the solid line, it forms a single bond or a double bond; in

5

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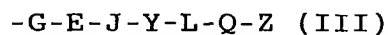
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group is preferred.

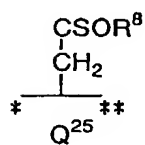
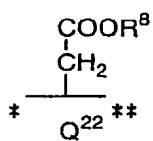
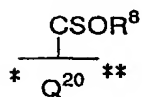
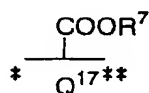
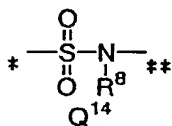
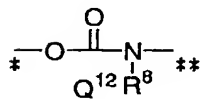
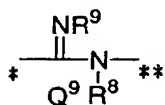
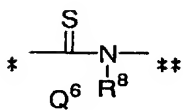
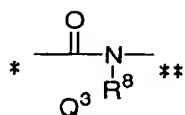
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R¹ represents an optionally substituted alkyl group, an optionally substituted alkenyl group or an optionally substituted alkynyl group; preferably, R¹ is R^{1a}

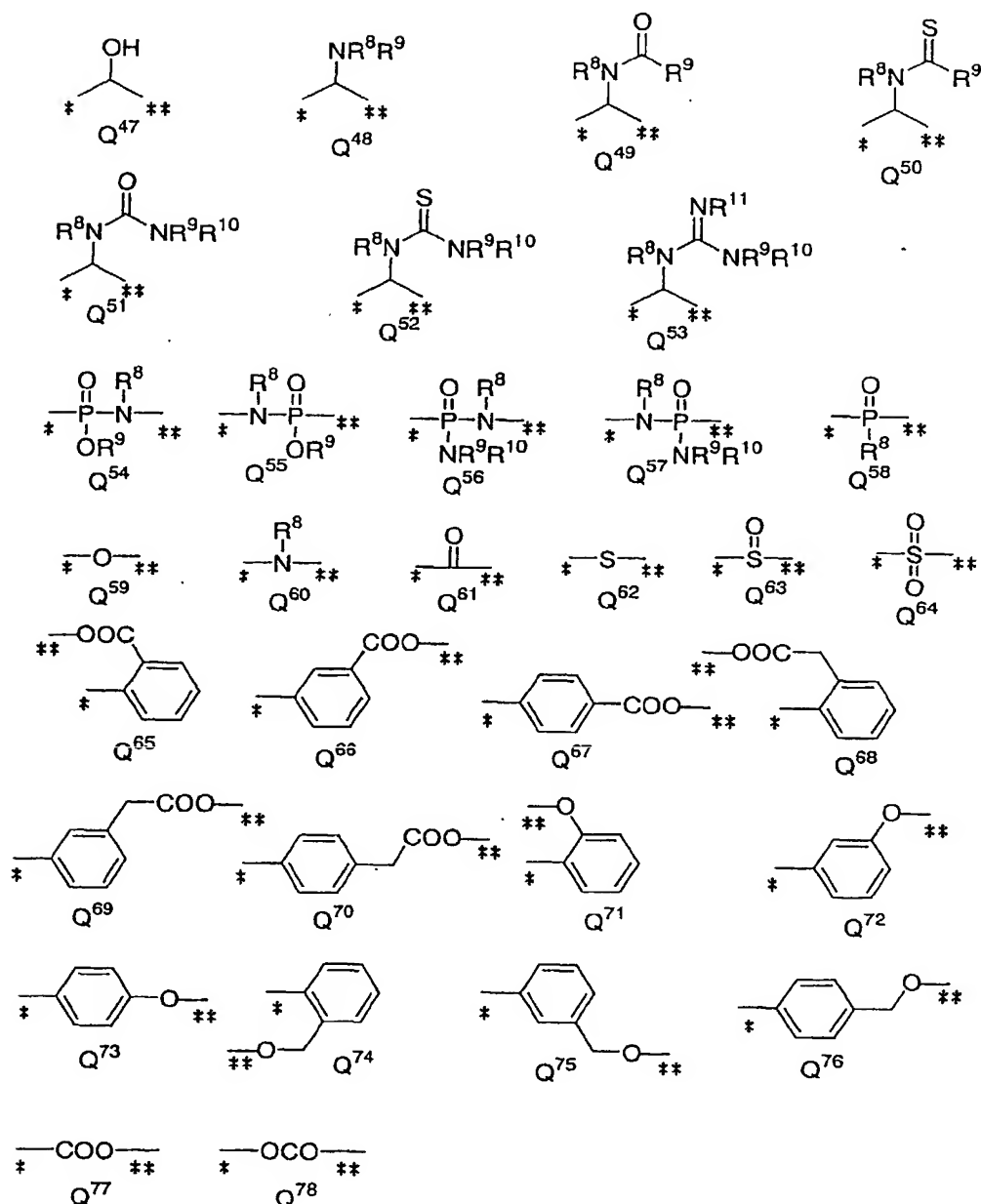
[where R^{1a} is the general formula (III)]



{wherein G represents an optionally substituted straight-chained or branched alkylene group having 1 - 30 carbon atoms, an optionally substituted straight-chained or branched alkenylene groups having 2 - 30 carbon atoms or an optionally substituted straight-chained or branched alkynylene group having 2 - 30 carbon atoms, E represents a single bond or -O-, J represents a single bond, an optionally substituted aromatic hydrocarbon group or an optionally substituted heterocyclic group, Y represents a single bond or -O-, L represents a single bond, a straight-chained or branched alkylene group having 1 - 10 carbon atoms, a straight-chained or branched alkenylene group having 2 - 10 carbon atoms or a straight-chained or branched alkynylene group having 2 - 10 carbon atoms, Q represents a single bond or one group selected from among the following formulae:







(where R⁷ and R⁸ represent independently a hydrogen atom or a straight-chained or branched lower alkyl group having 1 - 6 carbon atoms, R⁹, R¹⁰ and R¹¹ each independently represent a hydrogen atom or a straight-chained or branched lower alkyl group having 1 - 3 carbon atoms), Z represents a

hydrogen atom, a straight-chained or branched alkyl group having 1 - 10 carbon atoms that may optionally be substituted by a halogen atom, a straight-chained or branched alkenyl group having 2
 5 - 10 carbon atoms that may optionally be substituted by a halogen atom, a straight-chained or branched alkynyl group having 2 - 10 carbon atoms that may optionally be substituted by a halogen atom, $-O-R^d$ (where R^d represents a hydrogen atom or a protective group of a hydroxyl group),
 10 or $-COOH$), provided that when Q is Q^3 , the nitrogen atom and R^8 in Q^3 may combine with Z to form a heterocyclic group}}].

Examples of the substituent in G which G represents an optionally substituted straight-chained or branched
 15 alkylene group having 1 - 30 carbon atoms, an optionally substituted straight-chained or branched alkenylene group having 2 - 30 carbon atoms or an optionally substituted straight-chained or branched alkynylene group having 2 - 30 carbon atoms include $-(CH_2)_m-COOR^{7a}$, $-(CH_2)_p-CONR^{8a}R^{9a}$, $-NR^{8b}R^{9b}$,
 20 hydroxyl group, oxo group, etc. Here, m and p represent independently 0 or 1, R^{7a} represents a hydrogen atom or a straight-chained or branched alkyl group having 1 - 6 carbon atoms, R^{8a} , R^{9a} , R^{8b} and R^{9b} each independently represent a hydrogen atom or a straight-chained or branched
 25 alkyl group having 1 - 3 carbon atoms. The substituent is preferably absent or a hydroxyl group and its absence is particularly preferred. In the case where G is substituted, the number of substituents is from one to four, preferably

diyl group, 3-ethylpentane-1,5-diyl group, 3-ethyl-2-methylpentane-1,5-diyl group, 3-ethyl-4-methylpentane-1,5-diyl group, 2,4-dimethyl-3-ethylpentane-1,5-diyl group, 2-methylhexane-1,6-diyl group, 3-methylhexane-1,6-diyl group, 5 4-methylhexane-1,6-diyl group, 5-methylhexane-1,6-diyl group, 2,3-dimethylhexane-1,6-diyl group, 2,4-dimethylhexane-1,6-diyl group, 2,5-dimethylhexane-1,6-diyl group, 3,3-dimethylhexane-1,6-diyl group, 3,4-dimethylhexane-1,6-diyl group, 3,5-dimethylhexane-1,6-diyl 10 group, 4,4-dimethylhexane-1,6-diyl group, 4,5-dimethylhexane-1,6-diyl group, 2,3,3-trimethylhexane-1,6-diyl group, 2,3,4-trimethylhexane-1,6-diyl group, 2,3,5-trimethylhexane-1,6-diyl group, 2,4,4-trimethylhexane-1,6-diyl group, 2,4,5-trimethylhexane-1,6-diyl group, 3,3,4- 15 trimethylhexane-1,6-diyl group, 3,3,5-trimethylhexane-1,6-diyl group, 3,4,5-trimethylhexane-1,6-diyl group, 4,4,5-trimethylhexane-1,6-diyl group, 2,3,4,5-tetramethylhexane-1,6-diyl group, 3-ethylhexane-1,6-diyl group, 4-ethylhexane-1,6-diyl group, 3-ethyl-2-methylhexane-1,6-diyl 20 group, 3-ethyl-4-methylhexane-1,6-diyl group, 3-ethyl-5-methylhexane-1,6-diyl group, 4-ethyl-2-methylhexane-1,6-diyl group, 4-ethyl-3-methylhexane-1,6-diyl group, 4-ethyl-5-methylhexane-1,6-diyl group, 2,4-dimethyl-3-ethylhexane-1,6-diyl group, 2,5-dimethyl-3-ethylhexane-1,6-diyl group, 25 4,5-dimethyl-3-ethylhexane-1,6-diyl group, 2,3-dimethyl-4-ethylhexane-1,6-diyl group, 2,5-dimethyl-4-ethylhexane-1,6-diyl group, 3,5-dimethyl-4-ethylhexane-1,6-diyl group, 3,4-diethylhexane-1,6-diyl group;

- 2-methylheptane-1,7-diyl group, 3-methylheptane-1,7-diyl group, 4-methylheptane-1,7-diyl group, 5-methylheptane-1,7-diyl group, 6-methylheptane-1,7-diyl group, 2,3-dimethylheptane-1,7-diyl group, 2,4-dimethylheptane-1,7-diyl group, 2,5-dimethylheptane-1,7-diyl group, 2,6-dimethylheptane-1,7-diyl group, 3,3-dimethylheptane-1,7-diyl group, 3,4-dimethylheptane-1,7-diyl group, 3,5-dimethylheptane-1,7-diyl group, 3,6-dimethylheptane-1,7-diyl group, 4,4-dimethylheptane-1,7-diyl group, 4,5-dimethylheptane-1,7-diyl group, 4,6-dimethylheptane-1,7-diyl group, 5,5-dimethylheptane-1,7-diyl group, 5,6-dimethylheptane-1,7-diyl group, 2,3,3-trimethylheptane-1,7-diyl group, 2,3,4-trimethylheptane-1,7-diyl group, 2,3,5-trimethylheptane-1,7-diyl group, 2,3,6-trimethylheptane-1,7-diyl group, 2,4,4-trimethylheptane-1,7-diyl group, 2,4,5-trimethylheptane-1,7-diyl group, 2,4,6-trimethylheptane-1,7-diyl group, 2,5,5-trimethylheptane-1,7-diyl group, 2,5,6-trimethylheptane-1,7-diyl group, 3,3,4-trimethylheptane-1,7-diyl group, 3,3,5-trimethylheptane-1,7-diyl group, 3,3,6-trimethylheptane-1,7-diyl group, 3,4,4-trimethylheptane-1,7-diyl group, 3,4,5-trimethylheptane-1,7-diyl group, 3,4,6-trimethylheptane-1,7-diyl group, 3,5,5-trimethylheptane-1,7-diyl group, 3,5,6-trimethylheptane-1,7-diyl group, 4,4,5-trimethylheptane-1,7-diyl group, 4,4,6-trimethylheptane-1,7-diyl group, 4,5,5-trimethylheptane-1,7-diyl group, 4,5,6-trimethylheptane-1,7-diyl group, 3-ethylheptane-1,7-diyl group, 4-ethylheptane-1,7-diyl group,

- 5-ethylheptane-1,7-diyl group, 3-ethyl-2-methylheptane-1,7-diyl group, 3-ethyl-4-methylheptane-1,7-diyl group, 3-ethyl-5-methylheptane-1,7-diyl group, 3-ethyl-6-methylheptane-1,7-diyl group, 4-ethyl-2-methylheptane-1,7-diyl group, 4-ethyl-3-methylheptane-1,7-diyl group, 4-ethyl-4-methylheptane-1,7-diyl group, 4-ethyl-5-methylheptane-1,7-diyl group, 4-ethyl-6-methylheptane-1,7-diyl group, 5-ethyl-2-methylheptane-1,7-diyl group, 5-ethyl-3-methylheptane-1,7-diyl group, 5-ethyl-4-methylheptane-1,7-diyl group, 5-ethyl-5-methylheptane-1,7-diyl group, 5-ethyl-6-methylheptane-1,7-diyl group, 4-n-propylheptane-1,7-diyl group, 4-i-propylheptane-1,7-diyl group;
- 2-methyloctane-1,8-diyl group, 3-methyloctane-1,8-diyl group, 3-methyloctane-1,8-diyl group, 4-methyloctane-1,8-diyl group, 5-methyloctane-1,8-diyl group, 6-methyloctane-1,8-diyl group, 7-methyloctane-1,8-diyl group, 2,3-dimethyloctane-1,8-diyl group, 2,4-dimethyloctane-1,8-diyl group, 2,5-dimethyloctane-1,8-diyl group, 2,6-dimethyloctane-1,8-diyl group, 2,7-dimethyloctane-1,8-diyl group, 3,3-dimethyloctane-1,8-diyl group, 3,4-dimethyloctane-1,8-diyl group, 3,5-dimethyloctane-1,8-diyl group, 3,6-dimethyloctane-1,8-diyl group, 3,7-dimethyloctane-1,8-diyl group, 4,4-dimethyloctane-1,8-diyl group, 4,5-dimethyloctane-1,8-diyl group, 4,6-dimethyloctane-1,8-diyl group, 4,7-dimethyloctane-1,8-diyl group, 5,5-dimethyloctane-1,8-diyl group, 5,6-dimethyloctane-1,8-diyl group, 5,7-dimethyloctane-1,8-diyl

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ethyl-5-methyldecane-1,10-diyl group, 6-ethyl-5-methyl-
decane-1,10-diyl group, 7-ethyl-5-methyldecane-1,10-diyl
group;

2-methylundecane-1,11-diyl group, 3-methylundecane-1,11-
5 diyl group, 4-methylundecane-1,11-diyl group, 5-
methylundecane-1,11-diyl group, 6-methylundecane-1,11-diyl
group, 7-methylundecane-1,11-diyl group, 8-methylundecane-
1,11-diyl group, 9-methylundecane-1,11-diyl group, 10-
methylundecane-1,11-diyl group, 3-ethylundecane-1,11-diyl
10 group, 4-ethylundecane-1,11-diyl group, 5-ethylundecane-
1,11-diyl group, 6-ethylundecane-1,11-diyl group, 7-
ethylundecane-1,11-diyl group, 8-ethylundecane-1,11-diyl
group, 9-ethylundecane-1,11-diyl group;
2-methyldodecane-1,12-diyl group, 3-methyldodecane-1,12-
15 diyl group, 4-methyldodecane-1,12-diyl group, 5-
methyldodecane-1,12-diyl group, 6-methyldodecane-1,12-diyl
group, 7-methyldodecane-1,12-diyl group, 8-methyldodecane-
1,12-diyl group, 9-methyldodecane-1,12-diyl group, 10-
methyldodecane-1,12-diyl group, 11-methyldodecane-1,12-diyl
20 group;
3-ethyldodecane-1,12-diyl group, 4-ethyldodecane-1,12-diyl
group, 5-ethyldodecane-1,12-diyl group, 6-ethyldodecane-
1,12-diyl group, 7-ethyldodecane-1,12-diyl group, 8-
ethyldodecane-1,12-diyl group, 9-ethyldodecane-1,12-diyl
25 group, 10-ethyldodecane-1,12-diyl group;
2-methyltridecane-1,13-diyl group, 3-methyltridecane-1,13-
diyl group, 4-methyltridecane-1,13-diyl group, 5-
methyltridecane-1,13-diyl group, 6-methyltridecane-1,13-

5 diyl group;

10 1,13-diyl group, 10-ethyltridecane-1,13-diyl group, 11-ethyltridecane-1,13-diyl group;

15 1,14-diyl group, 7-methyltetradecane-1,14-diyl group, 8-methyltetradecane-1,14-diyl group, 9-methyltetradecane-1,14-diyl group, 10-methyltetradecane-1,14-diyl group, 11-methyltetradecane-1,14-diyl group, 12-methyltetradecane-1,14-diyl group, 13-methyltetradecane-1,14-diyl group;

25 diyl group, 11-ethyltetradecane-1,14-diyl group, 12-
ethyltetradecane-1,14-diyl group;

2-methylpentadecane-1,15-diyl group, 3-methylpentadecane-1,15-diyl group, 4-methylpentadecane-1,15-diyl group, 5-

- methylopentadecane-1,15-diyl group, 6-methylopentadecane-1,15-diyl group, 7-methylopentadecane-1,15-diyl group, 8-methylopentadecane-1,15-diyl group, 9-methylopentadecane-1,15-diyl group, 10-methylopentadecane-1,15-diyl group, 11-
- 5 methylopentadecane-1,15-diyl group, 12-methylopentadecane-1,15-diyl group, 13-methylopentadecane-1,15-diyl group, 14-methylopentadecane-1,15-diyl group;
- 3-ethylpentadecane-1,15-diyl group, 4-ethylpentadecane-1,15-diyl group, 5-ethylpentadecane-1,15-diyl group, 6-
- 10 ethylpentadecane-1,15-diyl group, 7-ethylpentadecane-1,15-diyl group, 8-ethylpentadecane-1,15-diyl group, 9-ethylpentadecane-1,15-diyl group, 10-ethylpentadecane-1,15-diyl group, 11-ethylpentadecane-1,15-diyl group, 12-ethylpentadecane-1,15-diyl group, 13-ethylpentadecane-1,15-
- 15 diyl group;
- 2-methylhexadecane-1,16-diyl group, 3-methylhexadecane-1,16-diyl group, 4-methylhexadecane-1,16-diyl group, 5-methylhexadecane-1,16-diyl group, 6-methylhexadecane-1,16-diyl group, 7-methylhexadecane-1,16-diyl group, 8-
- 20 methylhexadecane-1,16-diyl group, 9-methylhexadecane-1,16-diyl group, 10-methylhexadecane-1,16-diyl group, 11-methylhexadecane-1,16-diyl group, 12-methylhexadecane-1,16-diyl group, 13-methylhexadecane-1,16-diyl group, 14-methylhexadecane-1,16-diyl group, 15-methylhexadecane-1,16-
- 25 diyl group;
- 3-ethylhexadecane-1,16-diyl group, 4-ethylhexadecane-1,16-diyl group, 5-ethylhexadecane-1,16-diyl group, 6-ethylhexadecane-1,16-diyl group, 7-ethylhexadecane-1,16-

- diyl group, 8-ethylhexadecane-1,16-diyl group, 9-ethylhexadecane-1,16-diyl group, 10-ethylhexadecane-1,16-diyl group, 11-ethylhexadecane-1,16-diyl group, 12-ethylhexadecane-1,16-diyl group, 13-ethylhexadecane-1,16-diyl group, 14-ethylhexadecane-1,16-diyl group;
- 2-methylheptadecane-1,17-diyl group, 3-methylheptadecane-1,17-diyl group, 4-methylheptadecane-1,17-diyl group, 5-methylheptadecane-1,17-diyl group, 6-methylheptadecane-1,17-diyl group, 7-methylheptadecane-1,17-diyl group, 8-methylheptadecane-1,17-diyl group, 9-methylheptadecane-1,17-diyl group, 10-methylheptadecane-1,17-diyl group, 11-methylheptadecane-1,17-diyl group, 12-methylheptadecane-1,17-diyl group, 13-methylheptadecane-1,17-diyl group, 14-methylheptadecane-1,17-diyl group, 15-methylheptadecane-1,17-diyl group, 16-methylheptadecane-1,17-diyl group;
- 3-ethylheptadecane-1,17-diyl group, 4-ethylheptadecane-1,17-diyl group, 5-ethylheptadecane-1,17-diyl group, 6-ethylheptadecane-1,17-diyl group, 7-ethylheptadecane-1,17-diyl group, 8-ethylheptadecane-1,17-diyl group, 9-ethylheptadecane-1,17-diyl group, 10-ethylheptadecane-1,17-diyl group, 11-ethylheptadecane-1,17-diyl group, 12-ethylheptadecane-1,17-diyl group, 13-ethylheptadecane-1,17-diyl group, 14-ethylheptadecane-1,17-diyl group, 15-ethylheptadecane-1,17-diyl group;
- 2-methyloctadecane-1,18-diyl group, 3-methyloctadecane-1,18-diyl group, 4-methyloctadecane-1,18-diyl group, 5-methyloctadecane-1,18-diyl group, 6-methyloctadecane-1,18-diyl group, 7-methyloctadecane-1,18-diyl group, 8-

methyloctadecane-1,18-diyl group, 9-methyloctadecane-1,18-diyl group, 10-methyloctadecane-1,18-diyl group, 11-methyloctadecane-1,18-diyl group, 12-methyloctadecane-1,18-diyl group, 13-methyloctadecane-1,18-diyl group, 14-methyloctadecane-1,18-diyl group, 15-methyloctadecane-1,18-diyl group, 16-methyloctadecane-1,18-diyl group, 17-methyloctadecane-1,18-diyl group;

3-ethyloctadecane-1,18-diyl group, 4-ethyloctadecane-1,18-diyl group, 5-ethyloctadecane-1,18-diyl group, 6-ethyloctadecane-1,18-diyl group, 7-ethyloctadecane-1,18-diyl group, 8-ethyloctadecane-1,18-diyl group, 9-ethyloctadecane-1,18-diyl group, 10-ethyloctadecane-1,18-diyl group, 11-ethyloctadecane-1,18-diyl group, 12-ethyloctadecane-1,18-diyl group, 13-ethyloctadecane-1,18-diyl group, 14-ethyloctadecane-1,18-diyl group, 15-ethyloctadecane-1,18-diyl group, 16-ethyloctadecane-1,18-diyl group;

2-methylnonadecane-1,19-diyl group, 3-methylnonadecane-1,19-diyl group, 4-methylnonadecane-1,19-diyl group, 5-methylnonadecane-1,19-diyl group, 6-methylnonadecane-1,19-diyl group, 7-methylnonadecane-1,19-diyl group, 8-methylnonadecane-1,19-diyl group, 9-methylnonadecane-1,19-diyl group, 10-methylnonadecane-1,19-diyl group, 11-methylnonadecane-1,19-diyl group, 12-methylnonadecane-1,19-diyl group, 13-methylnonadecane-1,19-diyl group, 14-methylnonadecane-1,19-diyl group, 15-methylnonadecane-1,19-diyl group, 16-methylnonadecane-1,19-diyl group, 17-methylnonadecane-1,19-diyl group, 18-methylnonadecane-1,19-

diyl group;

3-ethylnonadecane-1,19-diyl group, 4-ethylnonadecane-1,19-diyl group, 5-ethylnonadecane-1,19-diyl group, 6-ethylnonadecane-1,19-diyl group, 7-ethylnonadecane-1,19-diyl group, 8-ethylnonadecane-1,19-diyl group, 9-ethylnonadecane-1,19-diyl group, 10-ethylnonadecane-1,19-diyl group, 11-ethylnonadecane-1,19-diyl group, 12-ethylnonadecane-1,19-diyl group, 13-ethylnonadecane-1,19-diyl group, 14-ethylnonadecane-1,19-diyl group, 15-ethylnonadecane-1,19-diyl group, 16-ethylnonadecane-1,19-diyl group, 17-ethylnonadecane-1,19-diyl group;

2-methylicosane-1,20-diyl group, 3-methylicosane-1,20-diyl group, 4-methylicosane-1,20-diyl group, 5-methylicosane-1,20-diyl group, 6-methylicosane-1,20-diyl group, 7-methylicosane-1,20-diyl group, 8-methylicosane-1,20-diyl group, 9-methylicosane-1,20-diyl group, 10-methylicosane-1,20-diyl group, 11-methylicosane-1,20-diyl group, 12-methylicosane-1,20-diyl group, 13-methylicosane-1,20-diyl group, 14-methylicosane-1,20-diyl group, 15-methylicosane-1,20-diyl group, 16-methylicosane-1,20-diyl group, 17-methylicosane-1,20-diyl group, 18-methylicosane-1,20-diyl group, 19-methylicosane-1,20-diyl group;

3-ethylicosane-1,20-diyl group, 4-ethylicosane-1,20-diyl group, 5-ethylicosane-1,20-diyl group, 6-ethylicosane-1,20-diyl group, 7-ethylicosane-1,20-diyl group, 8-ethylicosane-1,20-diyl group, 9-ethylicosane-1,20-diyl group, 10-ethylicosane-1,20-diyl group, 11-ethylicosane-1,20-diyl group, 12-ethylicosane-1,20-diyl group, 13-ethylicosane-

- 1,20-diyl group, 14-ethylicosane-1,20-diyl group, 15-ethylicosane-1,20-diyl group, 16-ethylicosane-1,20-diyl group, 17-ethylicosane-1,20-diyl group, 18-ethylicosane-1,20-diyl group;
- 5 2-methylhenicosane-1,21-diyl group, 3-methylhenicosane-1,21-diyl group, 4-methylhenicosane-1,21-diyl group, 5-methylhenicosane-1,21-diyl group, 6-methylhenicosane-1,21-diyl group, 7-methylhenicosane-1,21-diyl group, 8-methylhenicosane-1,21-diyl group, 9-methylhenicosane-1,21-diyl group,
- 10 10-methylhenicosane-1,21-diyl group, 11-methylhenicosane-1,21-diyl group, 12-methylhenicosane-1,21-diyl group, 13-methylhenicosane-1,21-diyl group, 14-methylhenicosane-1,21-diyl group, 15-methylhenicosane-1,21-diyl group, 16-methylhenicosane-1,21-diyl group, 17-methylhenicosane-1,21-diyl group, 18-methylhenicosane-1,21-diyl group, 19-methylhenicosane-1,21-diyl group, 20-methylhenicosane-1,21-diyl group;
- 15 3-ethylhenicosane-1,21-diyl group, 4-ethylhenicosane-1,21-diyl group, 5-ethylhenicosane-1,21-diyl group, 6-ethylhenicosane-1,21-diyl group, 7-ethylhenicosane-1,21-diyl group, 8-ethylhenicosane-1,21-diyl group, 9-ethylhenicosane-1,21-diyl group, 10-ethylhenicosane-1,21-diyl group, 11-ethylhenicosane-1,21-diyl group, 12-ethylhenicosane-1,21-diyl group, 13-ethylhenicosane-1,21-diyl group, 14-ethylhenicosane-1,21-diyl group, 15-ethylhenicosane-1,21-diyl group, 16-ethylhenicosane-1,21-diyl group, 17-ethylhenicosane-1,21-diyl group, 18-ethylhenicosane-1,21-diyl group, 19-ethylhenicosane-1,21-diyl group,
- 20 20-ethylhenicosane-1,21-diyl group;
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1,26-diyl group, 4-methylhexacosane-1,26-diyl group, 5-methylhexacosane-1,26-diyl group, 6-methylhexacosane-1,26-diyl group, 7-methylhexacosane-1,26-diyl group, 8-methylhexacosane-1,26-diyl group, 9-methylhexacosane-1,26-diyl group, 10-methylhexacosane-1,26-diyl group, 11-methylhexacosane-1,26-diyl group, 12-methylhexacosane-1,26-diyl group, 13-methylhexacosane-1,26-diyl group, 14-methylhexacosane-1,26-diyl group, 15-methylhexacosane-1,26-diyl group, 16-methylhexacosane-1,26-diyl group, 17-methylhexacosane-1,26-diyl group, 18-methylhexacosane-1,26-diyl group, 19-methylhexacosane-1,26-diyl group, 20-methylhexacosane-1,26-diyl group, 21-methylhexacosane-1,26-diyl group, 22-methylhexacosane-1,26-diyl group, 23-methylhexacosane-1,26-diyl group, 24-methylhexacosane-1,26-diyl group, 25-methylhexacosane-1,26-diyl group;

3-ethylhexacosane-1,26-diyl group, 4-ethylhexacosane-1,26-diyl group, 5-ethylhexacosane-1,26-diyl group, 6-ethylhexacosane-1,26-diyl group, 7-ethylhexacosane-1,26-diyl group, 8-ethylhexacosane-1,26-diyl group, 9-ethylhexacosane-1,26-diyl group, 10-ethylhexacosane-1,26-diyl group, 11-ethylhexacosane-1,26-diyl group, 12-ethylhexacosane-1,26-diyl group, 13-ethylhexacosane-1,26-diyl group, 14-ethylhexacosane-1,26-diyl group, 15-ethylhexacosane-1,26-diyl group, 16-ethylhexacosane-1,26-diyl group, 17-ethylhexacosane-1,26-diyl group, 18-ethylhexacosane-1,26-diyl group, 19-ethylhexacosane-1,26-diyl group, 20-ethylhexacosane-1,26-diyl group, 21-ethylhexacosane-1,26-diyl group, 22-ethylhexacosane-1,26-

- diyl group, 23-ethylhexacosane-1,26-diyl group, 24-ethylhexacosane-1,26-diyl group;
- 2-methylheptacosane-1,27-diyl group, 3-methylheptacosane-1,27-diyl group, 4-methylheptacosane-1,27-diyl group, 5-
- 5 methylheptacosane-1,27-diyl group, 6-methylheptacosane-1,27-diyl group, 7-methylheptacosane-1,27-diyl group, 8-methylheptacosane-1,27-diyl group, 9-methylheptacosane-1,27-diyl group, 10-methylheptacosane-1,27-diyl group, 11-methylheptacosane-1,27-diyl group, 12-methylheptacosane-
- 10 1,27-diyl group, 13-methylheptacosane-1,27-diyl group, 14-methylheptacosane-1,27-diyl group, 15-methylheptacosane-1,27-diyl group, 16-methylheptacosane-1,27-diyl group, 17-methylheptacosane-1,27-diyl group, 18-methylheptacosane-1,27-diyl group, 19-methylheptacosane-1,27-diyl group, 20-
- 15 methylheptacosane-1,27-diyl group, 21-methylheptacosane-1,27-diyl group, 22-methylheptacosane-1,27-diyl group, 23-methylheptacosane-1,27-diyl group, 24-methylheptacosane-1,27-diyl group, 25-methylheptacosane-1,27-diyl group, 26-methylheptacosane-1,27-diyl group;
- 20 3-ethylheptacosane-1,27-diyl group, 4-ethylheptacosane-1,27-diyl group, 5-ethylheptacosane-1,27-diyl group, 6-ethylheptacosane-1,27-diyl group, 7-ethylheptacosane-1,27-diyl group, 8-ethylheptacosane-1,27-diyl group, 9-ethylheptacosane-1,27-diyl group, 10-ethylheptacosane-1,27-
- 25 diyl group, 11-ethylheptacosane-1,27-diyl group, 12-ethylheptacosane-1,27-diyl group, 13-ethylheptacosane-1,27-diyl group, 14-ethylheptacosane-1,27-diyl group, 15-ethylheptacosane-1,27-diyl group, 16-ethylheptacosane-1,27-

diyl group, 17-ethylheptacosane-1,27-diyl group, 18-
 ethylheptacosane-1,27-diyl group, 19-ethylheptacosane-1,27-
 diyl group, 20-ethylheptacosane-1,27-diyl group, 21-
 ethylheptacosane-1,27-diyl group, 22-ethylheptacosane-1,27-
 5 diyl group, 23-ethylheptacosane-1,27-diyl group, 24-
 ethylheptacosane-1,27-diyl group, 25-ethylheptacosane-1,27-
 diyl group;
 2-methyloctacosane-1,28-diyl group, 3-methyloctacosane-
 1,28-diyl group, 4-methyloctacosane-1,28-diyl group, 5-
 10 methyloctacosane-1,28-diyl group, 6-methyloctacosane-1,28-
 diyl group, 7-methyloctacosane-1,28-diyl group, 8-
 methyloctacosane-1,28-diyl group, 9-methyloctacosane-1,28-
 diyl group, 10-methyloctacosane-1,28-diyl group, 11-
 methyloctacosane-1,28-diyl group, 12-methyloctacosane-1,28-
 15 diyl group, 13-methyloctacosane-1,28-diyl group, 14-
 methyloctacosane-1,28-diyl group, 15-methyloctacosane-1,28-
 diyl group, 16-methyloctacosane-1,28-diyl group, 17-
 methyloctacosane-1,28-diyl group, 18-methyloctacosane-1,28-
 diyl group, 19-methyloctacosane-1,28-diyl group, 20-
 20 methyloctacosane-1,28-diyl group, 21-methyloctacosane-1,28-
 diyl group, 22-methyloctacosane-1,28-diyl group, 23-
 methyloctacosane-1,28-diyl group, 24-methyloctacosane-1,28-
 diyl group, 25-methyloctacosane-1,28-diyl group, 26-
 methyloctacosane-1,28-diyl group, 27-methyloctacosane-1,28-
 25 diyl group;
 3-ethyloctacosane-1,28-diyl group, 4-ethyloctacosane-1,28-
 diyl group, 5-ethyloctacosane-1,28-diyl group, 6-
 ethyloctacosane-1,28-diyl group, 7-ethyloctacosane-1,28-

diyl group, 8-ethyloctacosane-1,28-diyl group, 9-ethyloctacosane-1,28-diyl group, 10-ethyloctacosane-1,28-diyl group, 11-ethyloctacosane-1,28-diyl group, 12-ethyloctacosane-1,28-diyl group, 13-ethyloctacosane-1,28-diyl group, 14-ethyloctacosane-1,28-diyl group, 15-ethyloctacosane-1,28-diyl group, 16-ethyloctacosane-1,28-diyl group, 17-ethyloctacosane-1,28-diyl group, 18-ethyloctacosane-1,28-diyl group, 19-ethyloctacosane-1,28-diyl group, 20-ethyloctacosane-1,28-diyl group, 21-ethyloctacosane-1,28-diyl group, 22-ethyloctacosane-1,28-diyl group, 23-ethyloctacosane-1,28-diyl group, 24-ethyloctacosane-1,28-diyl group, 25-ethyloctacosane-1,28-diyl group, 26-ethyloctacosane-1,28-diyl group; 2-methylnonacosane-1,29-diyl group, 3-methylnonacosane-1,29-diyl group, 4-methylnonacosane-1,29-diyl group, 5-methylnonacosane-1,29-diyl group, 6-methylnonacosane-1,29-diyl group, 7-methylnonacosane-1,29-diyl group, 8-methylnonacosane-1,29-diyl group, 9-methylnonacosane-1,29-diyl group, 10-methylnonacosane-1,29-diyl group, 11-methylnonacosane-1,29-diyl group, 12-methylnonacosane-1,29-diyl group, 13-methylnonacosane-1,29-diyl group, 14-methylnonacosane-1,29-diyl group, 15-methylnonacosane-1,29-diyl group, 16-methylnonacosane-1,29-diyl group, 17-methylnonacosane-1,29-diyl group, 18-methylnonacosane-1,29-diyl group, 19-methylnonacosane-1,29-diyl group, 20-methylnonacosane-1,29-diyl group, 21-methylnonacosane-1,29-diyl group, 22-methylnonacosane-1,29-diyl group, 23-methylnonacosane-1,29-diyl group, 24-methylnonacosane-1,29-

diyl group, 25-methylnonacosane-1,29-diyl group, 26-methylnonacosane-1,29-diyl group, 27-methylnonacosane-1,29-diyl group and 28-methylnonacosane-1,29-diyl group.

If G represents an optionally substituted straight-
 5 chained or branched alkenylene group having 2 - 30 carbon atoms, exemplary straight-chained or branched alkenylene groups having 2 - 30 carbon atoms include straight-chained alkenylene groups such as ethylene-1,2-diyl group, 1-propene-1,3-diyl group, 2-propene-1,3-diyl group, 1-butene-
 10 1,4-diyl group, 2-butene-1,4-diyl group, 3-butene-1,4-diyl group, 1,3-butadiene-1,4-diyl group, 2-pentene-1,5-diyl group, 3-pentene-1,5-diyl group, 2,4-pentadiene-1,5-diyl group, 2-hexene-1,6-diyl group, 3-hexene-1,6-diyl group, 4-hexene-1,6-diyl group, 2,4-hexadiene-1,6-diyl group, 2-
 15 heptene-1,7-diyl group, 3-heptene-1,7-diyl group, 4-heptene-1,7-diyl group, 5-heptene-1,7-diyl group, 2,4-heptadiene-1,7-diyl group, 2,5-heptadiene-1,7-diyl group, 3,5-heptadiene-1,7-diyl group, 2-octene-1,8-diyl group, 3-octene-1,8-diyl group, 4-octene-1,8-diyl group, 5-octene-
 20 1,8-diyl group, 6-octene-1,8-diyl group, 2,4-octadiene-1,8-diyl group, 2,5-octadiene-1,8-diyl group, 2,6-octadiene-1,8-diyl group, 2,4,6-octatriene-1,8-diyl group, 2-nonene-1,9-diyl group, 3-nonene-1,9-diyl group, 4-nonene-1,9-diyl group, 5-nonene-1,9-diyl group, 6-nonene-1,9-diyl group, 7-
 25 nonene-1,9-diyl group, 2-decene-1,10-diyl group, 3-decene-1,10-diyl group, 4-decene-1,10-diyl group, 5-decene-1,10-diyl group, 6-decene-1,10-diyl group, 7-decene-1,10-diyl group, 8-decene-1,10-diyl group;

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docosene-1,22-diyl group, 13-docosene-1,22-diyl group, 14-
docosene-1,22-diyl group, 15-docosene-1,22-diyl group, 16-
docosene-1,22-diyl group, 17-docosene-1,22-diyl group, 18-
docosene-1,22-diyl group, 19-docosene-1,22-diyl group, 20-
5 docosene-1,22-diyl group;
2-tricosene-1,23-diyl group, 3-tricosene-1,23-diyl group,
4-tricosene-1,23-diyl group, 5-tricosene-1,23-diyl group,
6-tricosene-1,23-diyl group, 7-tricosene-1,23-diyl group,
8-tricosene-1,23-diyl group, 9-tricosene-1,23-diyl group,
10 10-tricosene-1,23-diyl group, 11-tricosene-1,23-diyl group,
12-tricosene-1,23-diyl group, 13-tricosene-1,23-diyl group,
14-tricosene-1,23-diyl group, 15-tricosene-1,23-diyl group,
16-tricosene-1,23-diyl group, 17-tricosene-1,23-diyl group,
18-tricosene-1,23-diyl group, 19-tricosene-1,23-diyl group,
15 20-tricosene-1,23-diyl group, 21-tricosene-1,23-diyl group;
2-tetracosene-1,24-diyl group, 3-tetracosene-1,24-diyl
group, 4-tetracosene-1,24-diyl group, 5-tetracosene-1,24-
diyl group, 6-tetracosene-1,24-diyl group, 7-tetracosene-
1,24-diyl group, 8-tetracosene-1,24-diyl group, 9-
20 tetracosene-1,24-diyl group, 10-tetracosene-1,24-diyl group,
11-tetracosene-1,24-diyl group, 12-tetracosene-1,24-diyl
group, 13-tetracosene-1,24-diyl group, 14-tetracosene-1,24-
diyl group, 15-tetracosene-1,24-diyl group, 16-tetracosene-
1,24-diyl group, 17-tetracosene-1,24-diyl group, 18-
25 tetracosene-1,24-diyl group, 19-tetracosene-1,24-diyl group,
20-tetracosene-1,24-diyl group, 21-tetracosene-1,24-diyl
group, 22-tetracosene-1,24-diyl group;
2-pentacosene-1,25-diyl group, 3-pentacosene-1,25-diyl

- 1,27-diyl group, 8-heptacosene-1,27-diyl group, 9-heptacosene-1,27-diyl group, 10-heptacosene-1,27-diyl group, 11-heptacosene-1,27-diyl group, 12-heptacosene-1,27-diyl group, 13-heptacosene-1,27-diyl group, 14-heptacosene-1,27-diyl group, 15-heptacosene-1,27-diyl group, 16-heptacosene-1,27-diyl group, 17-heptacosene-1,27-diyl group, 18-heptacosene-1,27-diyl group, 19-heptacosene-1,27-diyl group, 20-heptacosene-1,27-diyl group, 21-heptacosene-1,27-diyl group, 22-heptacosene-1,27-diyl group, 23-heptacosene-1,27-diyl group, 24-heptacosene-1,27-diyl group, 25-heptacosene-1,27-diyl group;
- 2-octacosene-1,28-diyl group, 3-octacosene-1,28-diyl group, 4-octacosene-1,28-diyl group, 5-octacosene-1,28-diyl group, 6-octacosene-1,28-diyl group, 7-octacosene-1,28-diyl group, 8-octacosene-1,28-diyl group, 9-octacosene-1,28-diyl group, 10-octacosene-1,28-diyl group, 11-octacosene-1,28-diyl group, 12-octacosene-1,28-diyl group, 13-octacosene-1,28-diyl group, 14-octacosene-1,28-diyl group, 15-octacosene-1,28-diyl group, 16-octacosene-1,28-diyl group, 17-octacosene-1,28-diyl group, 18-octacosene-1,28-diyl group, 19-octacosene-1,28-diyl group, 20-octacosene-1,28-diyl group, 21-octacosene-1,28-diyl group, 22-octacosene-1,28-diyl group, 23-octacosene-1,28-diyl group, 24-octacosene-1,28-diyl group, 25-octacosene-1,28-diyl group, 26-octacosene-1,28-diyl group;
- 2-nonacosene-1,29-diyl group, 3-nonacosene-1,29-diyl group, 4-nonacosene-1,29-diyl group, 5-nonacosene-1,29-diyl group, 6-nonacosene-1,29-diyl group, 7-nonacosene-1,29-diyl group,

8-nonacosene-1,29-diyl group, 9-nonacosene-1,29-diyl group,
 10-nonacosene-1,29-diyl group, 11-nonacosene-1,29-diyl
 group, 12-nonacosene-1,29-diyl group, 13-nonacosene-1,29-
 diyl group, 14-nonacosene-1,29-diyl group, 15-nonacosene-
 5 1,29-diyl group, 16-nonacosene-1,29-diyl group, 17-
 nonacosene-1,29-diyl group, 18-nonacosene-1,29-diyl group,
 19-nonacosene-1,29-diyl group, 20-nonacosene-1,29-diyl
 group, 21-nonacosene-1,29-diyl group, 22-nonacosene-1,29-
 diyl group, 23-nonacosene-1,29-diyl group, 24-nonacosene-
 10 1,29-diyl group, 25-nonacosene-1,29-diyl group, 26-
 nonacosene-1,29-diyl group, 27-nonacosene-1,29-diyl group;
 2-triacontene-1,30-diyl group, 3-triacontene-1,30-diyl
 group, 4-triacontene-1,30-diyl group, 5-triacontene-1,30-
 diyl group, 6-triacontene-1,30-diyl group, 7-triacontene-
 15 1,30-diyl group, 8-triacontene-1,30-diyl group, 9-
 triacontene-1,30-diyl group, 10-triacontene-1,30-diyl group,
 11-triacontene-1,30-diyl group, 12-triacontene-1,30-diyl
 group, 13-triacontene-1,30-diyl group, 14-triacontene-1,30-
 diyl group, 15-triacontene-1,30-diyl group, 16-triacontene-
 20 1,30-diyl group, 17-triacontene-1,30-diyl group, 18-
 triacontene-1,30-diyl group, 19-triacontene-1,30-diyl group,
 20-triacontene-1,30-diyl group, 21-triacontene-1,30-diyl
 group, 22-triacontene-1,30-diyl group, 23-triacontene-1,30-
 diyl group, 24-triacontene-1,30-diyl group, 25-triacontene-
 25 1,30-diyl group, 26-triacontene-1,30-diyl group, 27-
 triacontene-1,30-diyl group, and 28-triacontene-1,30-diyl
 group;
 as well as branched alkenylene groups such as 1-

1,10-diyl group, 6-ethyl-4-methyl-8-decene-1,10-diyl group;
 6-methyl-2-undecene-1,11-diyl group, 4-ethyl-3-undecene-
 1,11-diyl group, 5-methyl-4-undecene-1,11-diyl group, 7-
 ethyl-5-undecene-1,11-diyl group, 5-methyl-6-undecene-1,11-
 5 diyl group, 9-ethyl-7-undecene-1,11-diyl group, 3-methyl-8-
 undecene-1,11-diyl group, 4-ethyl-9-undecene-1,11-diyl
 group;
 4-ethyl-2-dodecene-1,12-diyl group, 5-methyl-3-dodecene-
 1,12-diyl group, 6-ethyl-4-dodecene-1,12-diyl group, 7-
 10 methyl-5-dodecene-1,12-diyl group, 8-ethyl-6-dodecene-1,12-
 diyl group, 9-methyl-7-dodecene-1,12-diyl group, 10-ethyl-
 8-dodecene-1,12-diyl group, 2-methyl-9-dodecene-1,12-diyl
 group, 5-ethyl-10-dodecene-1,12-diyl group;
 4,7,9-trimethyl-2-tridecene-1,13-diyl group, 10-methyl-3-
 15 tridecene-1,13-diyl group, 8-ethyl-4-tridecene-1,13-diyl
 group, 4-methyl-5-tridecene-1,13-diyl group, 5-ethyl-6-
 tridecene-1,13-diyl group, 3,6-diethyl-7-tridecene-1,13-
 diyl group, 5-methyl-8-tridecene-1,13-diyl group, 7-ethyl-
 9-tridecene-1,13-diyl group, 4-methyl-10-tridecene-1,13-
 20 diyl group, 6-ethyl-11-tridecene-1,13-diyl group;
 7-methyl-2-tetradecene-1,14-diyl group, 8-ethyl-3-
 tetradecene-1,14-diyl group, 6-n-propyl-4-tetradecene-1,14-
 diyl group, 8-methyl-5-tetradecene-1,14-diyl group, 3-
 ethyl-6-tetradecene-1,14-diyl group, 10-methyl-7-
 25 tetradecene-1,14-diyl group, 6-i-propyl-8-tetradecene-1,14-
 diyl group, 5,7,11-trimethyl-9-tetradecene-1,14-diyl group,
 5-ethyl-10-tetradecene-1,14-diyl group, 6-methyl-11-
 tetradecene-1,14-diyl group, 4-n-butyl-12-tetradecene-1,14-

- propyl-5-icosene-1,20-diyl group, 12-methyl-6-icosene-1,20-diyl group, 11-ethyl-7-icosene-1,20-diyl group, 13-n-propyl-8-icosene-1,20-diyl group, 8-i-propyl-9-icosene-1,20-diyl group, 8-n-propyl-10-icosene-1,20-diyl group, 7-methyl-11-icosene-1,20-diyl group, 8-ethyl-12-icosene-1,20-diyl group, 10-n-propyl-13-icosene-1,20-diyl group, 9-i-propyl-14-icosene-1,20-diyl group, 10-n-butyl-15-icosene-1,20-diyl group, 8-s-butyl-16-icosene-1,20-diyl group, 7-i-butyl-17-icosene-1,20-diyl group, 9-methyl-18-icosene-1,20-diyl group;
- 11-methyl-2-henicosene-1,21-diyl group, 12-n-butyl-3-henicosene-1,21-diyl group, 10-n-pentyl-4-henicosene-1,21-diyl group, 8-ethyl-5-henicosene-1,21-diyl group, 10-i-propyl-6-henicosene-1,21-diyl group, 5-n-propyl-7-henicosene-1,21-diyl group, 13-n-butyl-8-henicosene-1,21-diyl group, 15-s-butyl-9-henicosene-1,21-diyl group, 5-methyl-10-henicosene-1,21-diyl group, 15-ethyl-6-methyl-11-henicosene-1,21-diyl group, 8-ethyl-12-henicosene-1,21-diyl group, 7-methyl-13-henicosene-1,21-diyl group, 11-ethyl-14-henicosene-1,21-diyl group, 6-ethyl-15-henicosene-1,21-diyl group, 9-methyl-16-henicosene-1,21-diyl group, 5-ethyl-9-methyl-17-henicosene-1,21-diyl group, 10,10-dimethyl-18-henicosene-1,21-diyl group, 9-ethyl-19-henicosene-1,21-diyl group;
- 11-methyl-2-docosene-1,22-diyl group, 12-ethyl-3-docosene-1,22-diyl group, 13-i-propyl-4-docosene-1,22-diyl group, 10-n-propyl-5-docosene-1,22-diyl group, 10-n-butyl-6-docosene-1,22-diyl group, 15-s-butyl-7-docosene-1,22-diyl

group, 11-i-butyl-8-docosene-1,22-diyl group, 5,15-
dimethyl-9-docosene-1,22-diyl group, 8,14-diethyl-10-
docosene-1,22-diyl group, 5-methyl-11-docosene-1,22-diyl
group, 7-ethyl-12-docosene-1,22-diyl group, 10-methyl-13-
5 docosene-1,22-diyl group, 10-ethyl-14-docosene-1,22-diyl
group, 9-ethyl-15-docosene-1,22-diyl group, 8-methyl-16-
docosene-1,22-diyl group, 7-i-propyl-17-docosene-1,22-diyl
group, 10-i-butyl-18-docosene-1,22-diyl group, 9,10-
dimethyl-19-docosene-1,22-diyl group, 13-ethyl-20-docosene-
10 1,22-diyl group;
19-methyl-2-tricosene-1,23-diyl group, 10,15-dimethyl-3-
tricosene-1,23-diyl group, 3,11,16-trimethyl-4-tricosene-
1,23-diyl group, 12-ethyl-5-tricosene-1,23-diyl group,
6,13-diethyl-6-tricosene-1,23-diyl group, 4,12,18-triethyl-
15 7-tricosene-1,23-diyl group, 18-i-propyl-8-tricosene-1,23-
diyl group, 14-n-propyl-9-tricosene-1,23-diyl group, 8-n-
butyl-10-tricosene-1,23-diyl group, 15-s-butyl-11-
tricosene-1,23-diyl group, 5-i-butyl-12-tricosene-1,23-diyl
group, 7-ethyl-9-methyl-13-tricosene-1,23-diyl group, 9-
20 methyl-14-tricosene-1,23-diyl group, 4,18-dimethyl-15-
tricosene-1,23-diyl group, 3,4,11-trimethyl-16-tricosene-
1,23-diyl group, 9-ethyl-17-tricosene-1,23-diyl group,
10,13-diethyl-18-tricosene-1,23-diyl group, 5,8,21-
triethyl-19-tricosene-1,23-diyl group, 15-i-propyl-20-
25 tricosene-1,23-diyl group, 17-n-propyl-21-tricosene-1,23-
diyl group;
16-n-butyl-2-tetracosene-1,24-diyl group, 11-s-butyl-3-
tetracosene-1,24-diyl group, 8-i-butyl-4-tetracosene-1,24-

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- pentacosene-1,25-diyl group, 5,22-dimethyl-18-pentacosene-1,25-diyl group, 5-i-butyl-19-pentacosene-1,25-diyl group, 9-methyl-13-ethyl-20-pentacosene-1,25-diyl group, 15-methyl-21-pentacosene-1,25-diyl group, 6,13-dimethyl-22-pentacosene-1,25-diyl group, 4,8,12-trimethyl-23-pentacosene-1,25-diyl group;
- 13-ethyl-2-hexacosene-1,26-diyl group, 5,16-diethyl-3-hexacosene-1,26-diyl group, 7,11,16-trimethyl-4-hexacosene-1,26-diyl group, 12-n-propyl-5-hexacosene-1,26-diyl group, 21-i-propyl-6-hexacosene-1,26-diyl group, 6-n-butyl-7-hexacosene-1,26-diyl group, 13-s-butyl-8-hexacosene-1,26-diyl group, 19-i-butyl-9-hexacosene-1,26-diyl group, 13-ethyl-18-methyl-10-hexacosene-1,26-diyl group, 10-methyl-11-hexacosene-1,26-diyl group, 10,20-dimethyl-12-hexacosene-1,26-diyl group, 7,9,17-trimethyl-13-hexacosene-1,26-diyl group, 8-ethyl-14-hexacosene-1,26-diyl group, 5,22-diethyl-15-hexacosene-1,26-diyl group, 7,10,21-trimethyl-16-hexacosene-1,26-diyl group, 15-n-propyl-17-hexacosene-1,26-diyl group, 13-i-propyl-18-hexacosene-1,26-diyl group, 8-n-butyl-19-hexacosene-1,26-diyl group, 11-s-butyl-20-hexacosene-1,26-diyl group, 14-i-butyl-21-hexacosene-1,26-diyl group, 5-ethyl-21-methyl-22-hexacosene-1,26-diyl group, 7-methyl-23-hexacosene-1,26-diyl group, 8,14-dimethyl-24-hexacosene-1,26-diyl group;
- 7,16,24-trimethyl-2-heptacosene-1,27-diyl group, 9-ethyl-3-heptacosene-1,27-diyl group, 7,16-dimethyl-4-heptacosene-1,27-diyl group, 9,13,21-trimethyl-5-heptacosene-1,27-diyl group, 13-n-propyl-6-heptacosene-1,27-diyl group, 10-i-

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chained or branched alkynylene group having 2 - 30 carbon atoms, exemplary straight-chained or branched alkynylene groups having 2 - 30 carbon atoms include straight-chained alkynylene groups such as acetylene-1,2-diyl group, 1-
5 propyne-1,3-diyl group, 2-propyne-1,3-diyl group, 1-butyne-1,4-diyl group, 2-butyne-1,4-diyl group, 3-butyne-1,4-diyl group, 1,3-butadiyne-1,4-diyl group, 2-pentyne-1,5-diyl group, 3-pentyne-1,5-diyl group, 2,4-pentadiyne-1,5-diyl group, 2-hexyne-1,6-diyl group, 3-hexyne-1,6-diyl group, 4-
10 hexyne-1,6-diyl group, 2,4-hexadiyne-1,6-diyl group, 2-heptyne-1,7-diyl group, 3-heptyne-1,7-diyl group, 4-heptyne-1,7-diyl group, 5-heptyne-1,7-diyl group, 2,4-heptadiyne-1,7-diyl group, 2,5-heptadiyne-1,7-diyl group, 3,5-heptadiyne-1,7-diyl group, 2-octyne-1,8-diyl group, 3-
15 octyne-1,8-diyl group, 4-octyne-1,8-diyl group, 5-octyne-1,8-diyl group, 6-octyne-1,8-diyl group, 2,4-octadiyne-1,8-diyl group, 2,5-octadiyne-1,8-diyl group, 2,6-octadiyne-1,8-diyl group, 2,4,6-octatriyne-1,8-diyl group, 2-nonyne-1,9-diyl group, 3-nonyne-1,9-diyl group, 4-nonyne-1,9-diyl
20 group, 5-nonyne-1,9-diyl group, 6-nonyne-1,9-diyl group, 7-nonyne-1,9-diyl group, 2-decyne-1,10-diyl group, 3-decyne-1,10-diyl group, 4-decyne-1,10-diyl group, 5-decyne-1,10-diyl group, 6-decyne-1,10-diyl group, 7-decyne-1,10-diyl group, 8-decyne-1,10-diyl group;
25 2-undecyne-1,11-diyl group, 3-undecyne-1,11-diyl group, 4-undecyne-1,11-diyl group, 5-undecyne-1,11-diyl group, 6-undecyne-1,11-diyl group, 7-undecyne-1,11-diyl group, 8-undecyne-1,11-diyl group, 9-undecyne-1,11-diyl group;





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- ethyl-6-methyl-2-heptyne-1,7-diyl group, 5-methyl-3-heptyne-1,7-diyl group, 3-n-propyl-4-heptyne-1,7-diyl group, 4,4-dimethyl-5-heptyne-1,7-diyl group, 6-methyl-2,4-heptadiyne-1,7-diyl group, 4-methyl-2,5-heptadiyne-1,7-diyl group, 2-methyl-3,5-heptadiyne-1,7-diyl group, 4-ethyl-6,6-dimethyl-2-octyne-1,8-diyl group, 5-n-propyl-3-octyne-1,8-diyl group, 3-ethyl-4-octyne-1,8-diyl group, 4-ethyl-2-methyl-5-octyne-1,8-diyl group, 3,4,5-trimethyl-6-octyne-1,8-diyl group, 7-methyl-2,4-octadiyne-1,8-diyl group, 4-methyl-2,5-octadiyne-1,8-diyl group, 5-n-propyl-2,6-octadiyne-1,8-diyl group, 5-ethyl-2-nonyne-1,9-diyl group, 5,6,7-trimethyl-3-nonyne-1,9-diyl group, 2,3,6,7-tetramethyl-4-nonyne-1,9-diyl group, 3,4-diethyl-5-nonyne-1,9-diyl group, 4-i-propyl-6-nonyne-1,9-diyl group, 3-ethyl-7-nonyne-1,9-diyl group, 5-n-butyl-2-decyne-1,10-diyl group, 6-i-propyl-3-decyne-1,10-diyl group, 7-ethyl-4-decyne-1,10-diyl group, 3,7-dimethyl-5-decyne-1,10-diyl group, 4-ethyl-6-decyne-1,10-diyl group, 5-methyl-7-decyne-1,10-diyl group, 6-ethyl-4-methyl-8-decyne-1,10-diyl group; 6-methyl-2-undecyne-1,11-diyl group, 6-ethyl-3-undecyne-1,11-diyl group, 7-methyl-4-undecyne-1,11-diyl group, 7-ethyl-5-undecyne-1,11-diyl group, 5-methyl-6-undecyne-1,11-diyl group, 9-ethyl-7-undecyne-1,11-diyl group, 3-methyl-8-undecyne-1,11-diyl group, 4-ethyl-9-undecyne-1,11-diyl group; 5-ethyl-2-dodecyne-1,12-diyl group, 6-methyl-3-dodecyne-1,12-diyl group, 8-ethyl-4-dodecyne-1,12-diyl group, 8-methyl-5-dodecyne-1,12-diyl group, 9-ethyl-6-dodecyne-1,12-

- diyl group, 6-methyl-7-dodecyne-1,12-diyl group, 10-ethyl-8-dodecyne-1,12-diyl group, 2-methyl-9-dodecyne-1,12-diyl group, 5-ethyl-10-dodecyne-1,12-diyl group, 4,7,9-trimethyl-2-tridecyne-1,13-diyl group, 10-methyl-3-tridecyne-1,13-diyl group, 8-ethyl-4-tridecyne-1,13-diyl group, 4-methyl-5-tridecyne-1,13-diyl group, 5-ethyl-6-tridecyne-1,13-diyl group, 3,6-diethyl-7-tridecyne-1,13-diyl group, 5-methyl-8-tridecyne-1,13-diyl group, 7-ethyl-9-tridecyne-1,13-diyl group, 4-methyl-10-tridecyne-1,13-diyl group, 6-ethyl-11-tridecyne-1,13-diyl group; 7-methyl-2-tetradecyne-1,14-diyl group, 8-ethyl-3-tetradecyne-1,14-diyl group, 6-n-propyl-4-tetradecyne-1,14-diyl group, 8-methyl-5-tetradecyne-1,14-diyl group, 3-ethyl-6-tetradecyne-1,14-diyl group, 10-methyl-7-tetradecyne-1,14-diyl group, 6-i-propyl-8-tetradecyne-1,14-diyl group, 5,7,11-trimethyl-9-tetradecyne-1,14-diyl group, 5-ethyl-10-tetradecyne-1,14-diyl group, 6-methyl-11-tetradecyne-1,14-diyl group, 4-n-butyl-12-tetradecyne-1,14-diyl group; 4-methyl-2-pentadecyne-1,15-diyl group, 6-ethyl-3-pentadecyne-1,15-diyl group, 8-methyl-4-pentadecyne-1,15-diyl group, 10-ethyl-5-pentadecyne-1,15-diyl group, 4,9-dimethyl-6-pentadecyne-1,15-diyl group, 10-ethyl-7-pentadecyne-1,15-diyl group, 6-methyl-8-pentadecyne-1,15-diyl group, 8-n-propyl-9-pentadecyne-1,15-diyl group, 5-methyl-10-pentadecyne-1,15-diyl group, 4,7-diethyl-11-pentadecyne-1,15-diyl group, 5-methyl-12-pentadecyne-1,15-diyl group, 8-ethyl-13-pentadecyne-1,15-diyl group;

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- 7-methyl-12-octadecyne-1,18-diyl group, 9-ethyl-13-octadecyne-1,18-diyl group, 10-i-propyl-14-octadecyne-1,18-diyl group, 7-methyl-15-octadecyne-1,18-diyl group, 10-ethyl-16-octadecyne-1,18-diyl group;
- 5 10-methyl-2-nonadecyne-1,19-diyl group, 10,12-diethyl-3-nonadecyne-1,19-diyl group, 7-methyl-4-nonadecyne-1,19-diyl group, 9-ethyl-5-nonadecyne-1,19-diyl group, 9-n-propyl-6-nonadecyne-1,19-diyl group, 10-methyl-7-nonadecyne-1,19-diyl group, 12-i-propyl-8-nonadecyne-1,19-diyl group, 5,15-
- 10 dimethyl-9-nonadecyne-1,19-diyl group, 7-ethyl-13-methyl-10-nonadecyne-1,19-diyl group, 6-methyl-11-nonadecyne-1,19-diyl group, 6-ethyl-12-nonadecyne-1,19-diyl group, 7,16-diethyl-13-nonadecyne-1,19-diyl group, 9-s-butyl-14-nonadecyne-1,19-diyl group, 8-methyl-15-nonadecyne-1,19-
- 15 diyl group, 10-ethyl-16-nonadecyne-1,19-diyl group, 10-i-propyl-17-nonadecyne-1,19-diyl group;
- 8-methyl-2-icosyne-1,20-diyl group, 6-ethyl-3-icosyne-1,20-diyl group, 10-i-propyl-4-icosyne-1,20-diyl group, 11-n-propoyl-5-icosyne-1,20-diyl group, 12-methyl-6-icosyne-
- 20 1,20-diyl group, 11-ethyl-7-icosyne-1,20-diyl group, 13-n-propyl-8-icosyne-1,20-diyl group, 6-i-propyl-9-icosyne-1,20-diyl group, 5-n-propyl-10-icosyne-1,20-diyl group, 7-methyl-11-icosyne-1,20-diyl group, 8-ethyl-12-icosyne-1,20-diyl group, 10-n-propyl-13-icosyne-1,20-diyl group, 9-i-
- 25 propyl-14-icosyne-1,20-diyl group, 10-n-butyl-15-icosyne-1,20-diyl group, 8-s-butyl-16-icosyne-1,20-diyl group, 7-i-butyl-17-icosyne-1,20-diyl group, 9-methyl-18-icosyne-1,20-diyl group;

11-methyl-2-henicosyne-1,21-diyl group, 12-n-butyl-3-henicosyne-1,21-diyl group, 10-n-pentyl-4-henicosyne-1,21-diyl group, 8-ethyl-5-henicosyne-1,21-diyl group, 10-i-propyl-6-henicosyne-1,21-diyl group, 5-n-propyl-7-henicosyne-1,21-diyl group, 13-n-butyl-8-henicosyne-1,21-diyl group, 15-s-butyl-9-henicosyne-1,21-diyl group, 5-methyl-10-henicosyne-1,21-diyl group, 15-ethyl-6-methyl-11-henicosyne-1,21-diyl group, 8-ethyl-12-henicosyne-1,21-diyl group, 7-methyl-13-henicosyne-1,21-diyl group, 11-ethyl-14-henicosyne-1,21-diyl group, 6-ethyl-15-henicosyne-1,21-diyl group, 9-methyl-16-henicosyne-1,21-diyl group, 5-ethyl-9-methyl-17-henicosyne-1,21-diyl group, 10,10-dimethyl-18-henicosyne-1,21-diyl group, 9-ethyl-19-henicosyne-1,21-diyl group);

11-methyl-2-docosyne-1,22-diyl group, 12-ethyl-3-docosyne-1,22-diyl group, 13-i-propyl-4-docosyne-1,22-diyl group, 10-n-propyl-5-docosyne-1,22-diyl group, 10-n-butyl-6-docosyne-1,22-diyl group, 15-s-butyl-7-docosyne-1,22-diyl group, 11-i-butyl-8-docosyne-1,22-diyl group, 5,15-dimethyl-9-docosyne-1,22-diyl group, 8,14-diethyl-10-docosyne-1,22-diyl group, 5-methyl-11-docosyne-1,22-diyl group, 7-ethyl-12-docosyne-1,22-diyl group, 10-methyl-13-docosyne-1,22-diyl group, 10-ethyl-14-docosyne-1,22-diyl group, 9-ethyl-15-docosyne-1,22-diyl group, 8-methyl-16-docosyne-1,22-diyl group, 7-i-propyl-17-docosyne-1,22-diyl group, 10-i-butyl-18-docosyne-1,22-diyl group, 9,10-dimethyl-19-docosyne-1,22-diyl group, 13-ethyl-20-docosyne-1,22-diyl group;

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- hexacosyne-1,26-diyl group, 13-s-butyl-8-hexacosyne-1,26-diyl group, 19-i-butyl-9-hexacosyne-1,26-diyl group, 13-ethyl-18-methyl-10-hexacosyne-1,26-diyl group, 10-methyl-11-hexacosyne-1,26-diyl group, 10,20-dimethyl-12-
- 5 hexacosyne-1,26-diyl group, 7,9,17-trimethyl-13-hexacosyne-1,26-diyl group, 8-ethyl-14-hexacosyne-1,26-diyl group, 5,22-diethyl-15-hexacosyne-1,26-diyl group, 7,10,21-trimethyl-16-hexacosyne-1,26-diyl group, 15-n-propyl-17-hexacosyne-1,26-diyl group, 13-i-propyl-18-hexacosyne-1,26-
- 10 diyl group, 8-n-butyl-19-hexacosyne-1,26-diyl group, 11-s-butyl-20-hexacosyne-1,26-diyl group, 14-i-butyl-21-hexacosyne-1,26-diyl group, 5-ethyl-21-methyl-22-hexacosyne-1,26-diyl group, 7-methyl-23-hexacosyne-1,26-diyl group, 8,14-dimethyl-24-hexacosyne-1,26-diyl group;
- 15 7,16,24-trimethyl-2-heptacosyne-1,27-diyl group, 9-ethyl-3-heptacosyne-1,27-diyl group, 7,16-dimethyl-4-heptacosyne-1,27-diyl group, 9,13,21-trimethyl-5-heptacosyne-1,27-diyl group, 13-n-propyl-6-heptacosyne-1,27-diyl group, 10-i-propyl-7-heptacosyne-1,27-diyl group, 16-n-propyl-8-
- 20 heptacosyne-1,27-diyl group, 18-methyl-9-heptacosyne-1,27-diyl group, 9-i-propyl-10-heptacosyne-1,27-diyl group, 15-ethyl-7-methyl-11-heptacosyne-1,27-diyl group, 25-methyl-12-heptacosyne-1,27-heptacosyne-1,27-diyl group, 8,21-dimethyl-13-heptacosyne-1,27-diyl group, 5,11,23-trimethyl-
- 25 14-heptacosyne-1,27-diyl group, 9-ethyl-15-heptacosyne-1,27-diyl group, 8,20-dimethyl-16-heptacosyne-1,27-diyl group, 4,8,19-trimethyl-17-heptacosyne-1,27-diyl group, 7-n-propyl-18-heptacosyne-1,27-diyl group, 21-i-propyl-19-

heptacosyne-1,27-diyl group, 14-n-propyl-20-heptacosyne-
 1,27-diyl group, 8-ethyl-21-heptacosyne-1,27-diyl group,
 11-i-propyl-22-heptacosyne-1,27-diyl group, 5-ethyl-13-
 methyl-23-heptacosyne-1,27-diyl group, 16-methyl-24-
 5 heptacosyne-1,27-diyl group, 7-ethyl-25-heptacosyne-1,27-
 diyl group;
 14-ethyl-2-octacosyne-1,28-diyl group, 20-methyl-3-
 octacosyne-1,28-diyl group, 7,22-dimethyl-4-octacosyne-
 1,28-diyl group, 19-ethyl-5-octacosyne-1,28-diyl group, 11-
 10 methyl-6-octacosyne-1,28-diyl group, 13,16-dimethyl-7-
 octacosyne-1,28-diyl group, 13-ethyl-8-octacosyne-1,28-diyl
 group, 6-methyl-9-octacosyne-1,28-diyl group, 9,16-
 dimethyl-10-octacosyne-1,28-diyl group, 7-ethyl-11-
 octacosyne-1,28-diyl group, 16-methyl-12-octacosyne-1,28-
 15 diyl group, 6,15-dimethyl-13-octacosyne-1,28-diyl group,
 22-ethyl-14-octacosyne-1,28-diyl group, 6-methyl-15-
 octacosyne-1,28-diyl group, 8,11-dimethyl-16-octacosyne-
 1,28-diyl group, 23-ethyl-17-octacosyne-1,28-diyl group, 4-
 methyl-18-octacosyne-1,28-diyl group, 7,14-dimethyl-19-
 20 octacosyne-1,28-diyl group, 13-ethyl-20-octacosyne-1,28-
 diyl group, 8-methyl-21-octacosyne-1,28-diyl group, 11,17-
 dimethyl-22-octacosyne-1,28-diyl group, 10-ethyl-23-
 octacosyne-1,28-diyl group, 9-methyl-24-octacosyne-1,28-
 diyl group, 7,19-dimethyl-25-octacosyne-1,28-diyl group,
 25 12-ethyl-26-octacosyne-1,28-diyl group;
 15-methyl-2-nonacosyne-1,29-diyl group, 14-methyl-3-
 nonacosyne-1,29-diyl group, 12-methyl-4-nonacosyne-1,29-
 diyl group, 13-methyl-5-nonacosyne-1,29-diyl group, 11-

methyl-6-nonacosyne-1,29-diyl group, 10-methyl-7-
 nonacosyne-1,29-diyl group, 25-methyl-8-nonacosyne-1,29-
 diyl group, 24-methyl-9-nonacosyne-1,29-diyl group, 23-
 methyl-10-nonacosyne-1,29-diyl group, 22-methyl-11-
 5 nonacosyne-1,29-diyl group, 21-methyl-12-nonacosyne-1,29-
 diyl group, 20-methyl-13-nonacosyne-1,29-diyl group, 19-
 methyl-14-nonacosyne-1,29-diyl group, 18-methyl-15-
 nonacosyne-1,29-diyl group, 27-methyl-16-nonacosyne-1,29-
 diyl group, 26-methyl-17-nonacosyne-1,29-diyl group, 25-
 10 methyl-18-nonacosyne-1,29-diyl group, 24-methyl-19-
 nonacosyne-1,29-diyl group, 23-methyl-20-nonacosyne-1,29-
 diyl group, 20-methyl-21-nonacosyne-1,29-diyl group, 19-
 methyl-22-nonacosyne-1,29-diyl group, 18-methyl-23-
 nonacosyne-1,29-diyl group, 17-methyl-24-nonacosyne-1,29-
 15 diyl group, 16-methyl-25-nonacosyne-1,29-diyl group, 6-
 methyl-26-nonacosyne-1,29-diyl group, and 5-methyl-27-
 nonacosyne-1,29-diyl group.

Typically, optionally substituted straight-chained
 alkylene groups having 1 - 30 carbon atoms are preferred as
 20 G; optionally substituted straight-chained groups having 2
 - 15 carbon atoms are more preferred and straight-chained
 alkylene groups having 2 - 13 carbon atoms that may
 optionally be substituted by a hydroxyl group are further
 preferred; among these, ethane-1,2-diyl group, propane-1,3-
 25 diyl group, butane-1,4-diyl group, pentane-1,5-diyl group,
 hexane-1,6-diyl group, heptane-1,7-diyl group, octane-1,8-
 diyl group, nonane-1,9-diyl group, decane-1,10-diyl group,
 undecane-1,11-diyl group, dodecane-1,12-diyl group,

tridecane-1,13-diyl group, 2-hydroxypropane-1,3-diyl group, 3-hydroxy-octane-1,8-diyl group, 3-hydroxynonane-1,9-diyl group, 3-hydroxydecane-1,10-diyl group and the like are particularly preferred.

5 The optionally substituted straight-chained or branched alkylene group having 1 - 30 carbon atoms, the optionally substituted straight-chained or branched alkenylene group having 2 - 30 carbon atoms and the optionally substituted straight-chained or branched
10 alkynylene group having 2 - 30 carbon atoms, all being listed as candidates for G, are such that they bind to A in their 1-position and bind to E in their ω position or bind to E in their 1-position and bind to A in their ω position; preferably, they bind to A in their 1-position and bind to
15 E in their ω position.

E represents a single bond or -O- and preferably represents a single bond.

J represents a single bond, an optionally substituted aromatic hydrocarbon group or an optionally substituted
20 heterocyclic group, with a single bond and an aromatic hydrocarbon group being preferred, and a single bond being more preferred.

If J is an optionally substituted aromatic hydrocarbon group or an optionally substituted heterocyclic group,
25 exemplary substituents include $-(CH_2)_k-COOR^{7b}$, $-(CH_2)_l-$, $CONR^{8c}R^{9c}$, $-NR^{8d}R^{9d}$, hydroxyl group, etc. Here, k and l represent independently 0 or 1; R^{7b} represents a hydrogen atom or a straight-chained or branched alkyl group having 1

- 6 carbon atoms; R^{8c} , R^{9c} , R^{8c} and R^{9d} represent each independently a hydrogen atom or a straight-chained or branched alkyl group having 1 - 3 carbon atoms. Except in the case where Q is a single bond, these substituents are preferably absent and in the case where Q is a single bond, a preferred substituent is $-(CH_2)_k-COOR^{7b}$ (where k and R^{7b} have the same meanings as defined above). In the case where J is substituted, the number of substituents is from one to four, preferably one.

10 If J is an optionally substituted aromatic hydrocarbon group, the definition of the aromatic hydrocarbon group is the same as given for the aromatic hydrocarbon group in the case where it is used as Ar; preferred examples include p-phenylene group and m-phenylene group.

15 If J is an optionally substituted aromatic hydrocarbon group, preferred examples are unsubstituted p-phenylene group, unsubstituted m-phenylene group and -COOH substituted phenylene group.

If J is an optionally substituted heterocyclic group, 20 the heterocyclic group means a 4-membered to 10-membered monocyclic or fused aliphatic or aromatic ring containing 1 - 4 hetero atoms which may be the same or different and are exemplified by an oxygen atom, a nitrogen atom and a sulfur atom; specific examples include oxetane, furan, 25 dihydrofuran, tetrahydrofuran, pyran, dihydropyran, tetrahydropyran, dioxole, thiophene, dihydrothiophene, tetrahydrothiophene, thiopyran, dihydrothiopyran, tetrahydrothiopyran, pyrrole, dihydropyrrole, pyrrolidine,

pyridine, dihydropyridine, tetrahydropyridine, piperidine,
pyrazole, 2-pyrazoline, pyrazolidine, imidazole,
imidazolidine, pyrimidine, pyrazine, pyridazine, oxazoline,
piperazine, 1,2,3-triazole, 1,2,4-triazole, tetrazole,
5 isoxazole, 1,3-oxazole, 1,2,3-oxadiazole, 1,2,4-oxadiazole,
1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2-thiazole, 1,3-
thiazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-
thiadiazole, 1,3,4-thiadiazole, 1,3-dioxolan, 1,4-dioxane,
oxazolidine, morpholine, indole, quinoline, isoquinoline,
10 benzopyran, benzofuran, benzothiophene, benzodiazole,
benzoxazole and benzothiazole. Preferred examples include
furan and oxazole. The heterocyclic group as J means a
group having one bond each in two different positions in
these hetero rings other than the positions having
15 substituents; preferred examples include furan-2,5-diyl
group, 1,3-oxazole-2,4-diyl group and 1,3-oxazole-2,5-diyl
group.

Preferred examples of the optionally substituted
heterocyclic group as J include unsubstituted furan-2,5-
20 diyl group, unsubstituted 1,3-oxazole-2,4-diyl group and
unsubstituted 1,3-oxazole-2,5-diyl group.

If J is an optionally substituted aromatic hydrocarbon
group or an optionally substituted heterocyclic group, it
may be bound to E via any of the two bonds as long as it is
25 bound to E via one bond and bound to Y via the other;
preferably, J is bound to E in 4-position if it is 1,3-
oxazole-2,4-diyl group and bound to E in 5-position if it
is 1,3-oxazole-2,5-diyl group.

Y represents a single bond or -O- and preferably represents a single bond.

L represents a single bond, a straight-chained or branched alkylene group having 1 - 10 carbon atoms, a
5 straight-chained or branched alkenylene group having 2 - 10 carbon atoms or a straight-chained or branched alkynylene group having 2 - 10 carbon atoms and a single bond is preferred; if J is an optionally substituted aromatic hydrocarbon group and Y is a single bond, L is preferably a
10 single bond or a straight-chained alkylene group having 1 - 5 carbon atoms, among which a single bond and a straight-chained alkylene group having 1 - 3 carbon atoms are preferred, with a single bond and propane-1,3-dily group being particularly preferred; if J is an optionally
15 substituted aromatic hydrocarbon group and Y is -O-, L is preferably one of straight-chained alkylene groups having 1 - 5 carbon atoms, among which straight-chained alkylene groups having 2 - 4 carbon atoms are preferred.

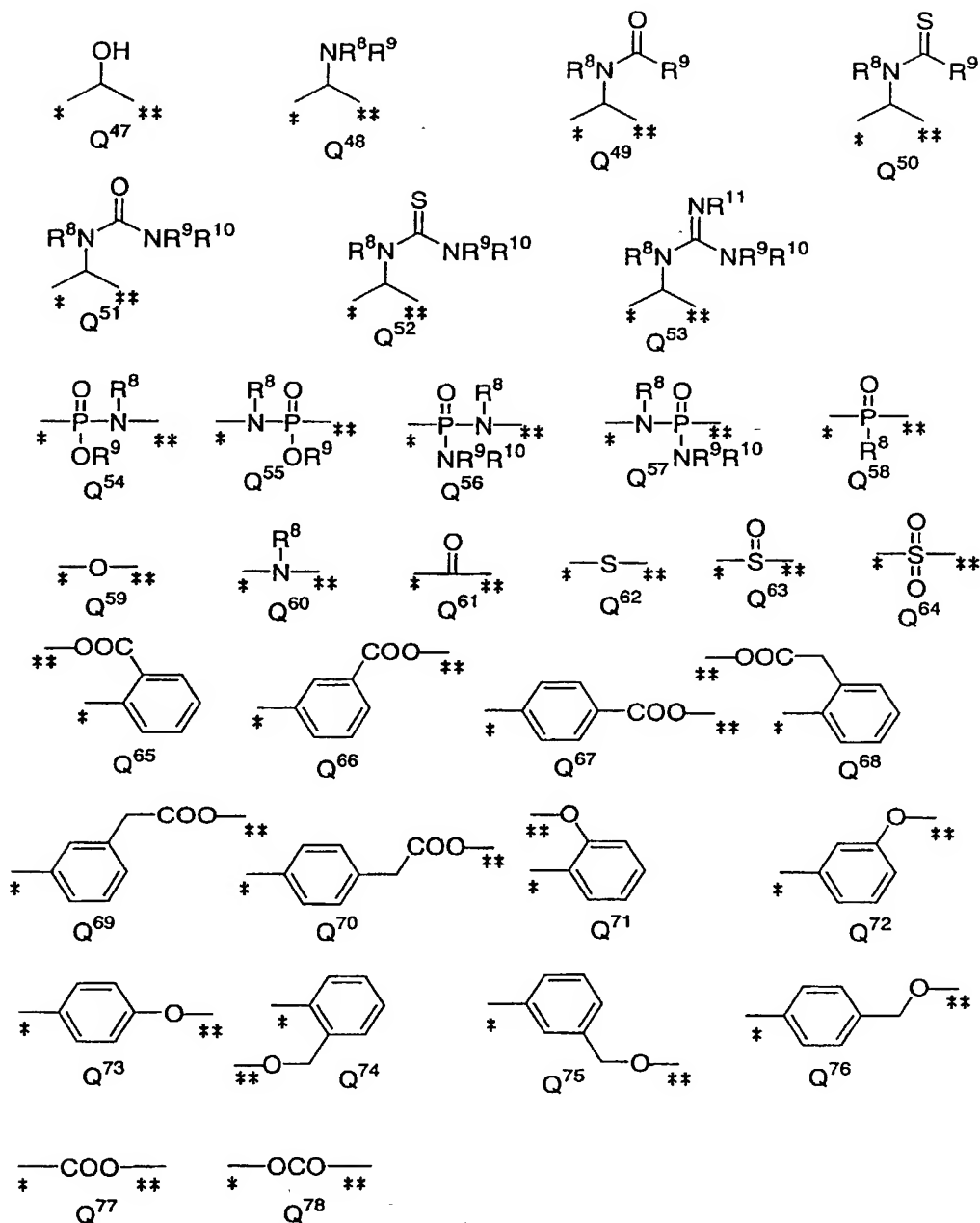
L represents a straight-chained or branched alkylene
20 group having 1 - 10 carbon atoms, a straight-chained or branched alkenylene group having 2 - 10 carbon atoms, a straight-chained or branched alkynylene group having 2 - 10 carbon atoms, a straight-chained alkylene group having 1 - 5 carbon atoms, a straight-chained alkylene group having 1
25 - 3 carbon atoms or a straight-chained alkylene group having 2 - 4 carbon atoms; specific examples of these groups can appropriately be selected from the list of specific examples of G which represents an optionally

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substituted straight-chained or branched alkylene group having 1 - 30 carbon atoms, an optionally substituted straight-chained or branched alkenylene group having 2 - 30 carbon atoms or an optionally substituted straight-chained or branched alkynylene group having 2 - 30 carbon atoms, except that methylene group is added to the list.

Any of the two bonds of L may be bound to Y as long as it satisfies the condition that it is bound to Y via one bond and bound to Q via the other.

10 Q represents a single bond or one group selected from among the following formulae:



(where R^7 represents a hydrogen atom or a straight-chained or branched lower alkyl group having 1 - 6 carbon atoms, and R^8 R^9 , R^{10} and R^{11} represent each independently a

5 hydrogen atom or a straight-chained or branched lower alkyl

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group having 1 - 3 carbon atoms); Q is preferably Q² {where examples of Q² include a single bond, Q⁶², Q⁶³, Q⁶⁴, Q³ (where R⁸ has the same meaning as defined above), Q⁴ (where R⁸ has the same meaning as defined above), Q¹⁷ (where R⁷ has the same meaning as defined above), Q³² (where R⁷ has the same meaning as defined above) and Q²⁷ (where R⁷ has the same meaning as defined above)}; considering the strength of antiandrogenic activity, cases where Q is Q⁶², Q⁶³, Q⁶⁴ and Q³, as well as Q⁴ where R⁸ is a hydrogen atom are more preferred, with Q⁶², Q⁶³, Q⁶⁴ and Q³ being particularly preferred. If Q is Q³, the nitrogen atom and R⁸ in Q³ may preferably combine with Z to form a heterocyclic group. Considering peroral absorption, Q is more preferably Q¹⁷ where R⁷ is a hydrogen atom, or Q³² where R⁷ is a hydrogen atom, or Q²⁷ where R⁷ is a hydrogen atom. If Z is -COOH, Q may preferably be a single bond considering peroral absorption.

Further referring to Q, it is bound to L in the position marked with * and bound to Z in the position marked with **.

Z represents a hydrogen atom, an optionally substituted straight-chained or branched alkyl group having 1 - 10 carbon atoms, a straight-chained or branched alkenyl group having 2 - 10 carbon atoms that may optionally be substituted by a cycloalkyl group having 3 - 6 carbon atoms or a halogen atom, a straight-chained or branched alkynyl group having 2 - 10 carbon atoms that may optionally be

substituted by a halogen atom, $-O-R^d$ (where R^d represents a hydrogen atom or a protective group of a hydroxyl group), or $-COOH$.

If Z is an optionally substituted straight-chained or
5 branched alkyl group having 1 - 10 carbon atoms, exemplary
substituents include a halogen atom, a cycloalkyl group, a
phenyl group optionally substituted by a straight-chained
or branched alkyl group, a heterocyclic group, and a
hydroxyl group. Said heterocyclic group may be exemplified
10 by a furyl group. Examples of said halogen atom include a
fluorine atom, a chlorine atom, a bromine atom and an
iodine atom, with a fluorine atom being preferred. If said
optionally substituted straight-chained or branched alkyl
group having 1 - 10 carbon atoms is substituted by a
15 halogen atom, the number of substituent halogen atoms
ranges from one to ten, preferably from three to nine, and
substitution by five halogen atoms is particularly
preferred. In a preferred mode of substitution, all
hydrogen atoms on a certain carbon atom are substituted by
20 halogen atoms (as in the cases of trihalomethyl group,
1,1,3,3,3-pentahalopropyl group, etc.)

If Z is a straight-chained or branched alkenyl group
having 2 - 10 carbon atoms that may optionally be
substituted by a halogen atom or a straight-chained or
25 branched alkynyl group having 2 - 10 carbon atoms that may
optionally be substituted by a halogen atom, exemplary
halogen atoms include a fluorine atom, a chlorine atom, a
bromine atom and an iodine atom, with a fluorine atom being

preferred. The number of substituent halogen atoms ranges from one to ten, preferably from three to nine, and substitution by five halogen atoms is particularly preferred. In a preferred mode of substitution, all hydrogen atoms on a certain carbon atom are substituted by halogen atoms.

If Z is an optionally substituted straight-chained or branched alkyl group having 1 - 10 carbon atoms, exemplary straight-chained or branched alkyl groups having 1 - 10 carbon atoms include straight-chained alkyl groups, i.e., methyl group, ethyl group, n-propyl group, n-butyl group, n-pentyl group, n-hexyl group, n-heptyl group, n-octyl group, n-nonyl group and n-decyl group, as well as branched alkyl groups such as 1-methylethyl group, 1-methylpropyl group, 2-methylpropyl group, 1-methylbutyl group, 2-methylbutyl group, 3-methylbutyl group, 1,1-dimethylpropyl group, 1,2-dimethylpropyl group, 2,2-dimethylpropyl group, 1-ethylpropyl group, 1-methylpentyl group, 2-methylpentyl group, 3-methylpentyl group, 4-methylpentyl group, 1,1-dimethylbutyl group, 1,2-dimethylbutyl group, 1,3-dimethylbutyl group, 2,2-dimethylbutyl group, 2,3-dimethylbutyl group, 3,3-dimethylbutyl group, 1-ethylbutyl group, 2-ethylbutyl group, 1-methylhexyl group, 2-methylhexyl group, 3-methylhexyl group, 4-methylhexyl group, 5-methylhexyl group, 1-ethylpentyl group, 2-ethylpentyl group, 3-ethylpentyl group, 1,1-dimethylpentyl group, 1,2-dimethylpentyl group, 1,3-dimethylpentyl group, 1,4-dimethylpentyl group, 2,2-dimethylpentyl group, 2,3-

dimethylpentyl group, 2,4-dimethylpentyl group, 3,3-dimethylpentyl group, 3,4-dimethylpentyl group, 3,3-dimethylpentyl group, 3,4-dimethylpentyl group, 4,4-dimethylpentyl group, 1-propylbutyl group, 1-ethyl-1-methylbutyl group, 1-ethyl-2-methylbutyl group, 1-ethyl-3-methylbutyl group, 2-ethyl-1-methylbutyl group, 2-ethyl-2-methylbutyl group, 2-ethyl-3-methylbutyl group, 1,1,2-trimethylbutyl group, 1,1,3-trimethylbutyl group, 1,2,2-trimethylbutyl group, 1,2,3-trimethylbutyl group, 1,3,3-trimethylbutyl group, 2,2,3-trimethylbutyl group, 2,3,3-trimethylbutyl group, 1-methylheptyl group, 2-methylheptyl group, 3-methylheptyl group, 4-methylheptyl group, 5-methylheptyl group, 6-methylheptyl group, 1-ethylhexyl group, 2-ethylhexyl group, 3-ethylhexyl group, 4-ethylhexyl group, 1,1-dimethylhexyl group, 1,2-dimethylhexyl group, 1,3-dimethylhexyl group, 1,4-dimethylhexyl group, 1,5-dimethylhexyl group, 2,2-dimethylhexyl group, 2,3-dimethylhexyl group, 2,4-dimethylhexyl group, 2,5-dimethylhexyl group, 3,3-dimethylhexyl group, 3,4-dimethylhexyl group, 3,5-dimethylhexyl group, 4,4-dimethylhexyl group, 4,5-dimethylhexyl group, 5,5-dimethylhexyl group;

1-propylpentyl group, 2-propylpentyl group, 1-ethyl-1-methylpentyl group, 1-ethyl-2-methylpentyl group, 1-ethyl-3-methylpentyl group, 1-ethyl-4-methylpentyl group, 2-ethyl-1-methylpentyl group, 2-ethyl-2-methylpentyl group, 2-ethyl-3-methylpentyl group, 2-ethyl-4-methylpentyl group, 3-ethyl-1-methylpentyl group, 3-ethyl-2-methylpentyl group,

- 3-ethyl-3-methylpentyl group, 3-ethyl-4-methylpentyl group,
 1,1,2-trimethylpentyl group, 1,1,3-trimethylpentyl group,
 1,1,4-trimethylpentyl group, 1,2,2-trimethylpentyl group,
 1,2,3-trimethylpentyl group, 1,2,4-trimethylpentyl group,
 5 1,3,3-trimethylpentyl group, 1,3,4-trimethylpentyl group,
 1,4,4-trimethylpentyl group, 2,2,3-trimethylpentyl group,
 2,2,4-trimethylpentyl group, 2,3,3-trimethylpentyl group,
 2,3,4-trimethylpentyl group, 2,4,4-trimethylpentyl group,
 3,3,4-trimethylpentyl group, 3,4,4-trimethylpentyl group,
 10 1-methyl-1-propylbutyl group, 2-methyl-1-propylbutyl group,
 3-methyl-1-propylbutyl group, 1,1-diethylbutyl group, 1,2-
 diethylbutyl group, 2,2-diethylbutyl group, 1,2-dimethyl-1-
 ethylbutyl group, 1,3-dimethyl-1-ethylbutyl group, 2,2-
 dimethyl-1-ethylbutyl group, 2,3-dimethyl-1-ethylbutyl
 15 group, 3,3-dimethyl-1-ethylbutyl group, 1,1-dimethyl-2-
 ethylbutyl group, 1,2-dimethyl-2-ethylbutyl group, 1,3-
 dimethyl-2-ethylbutyl group, 2,3-dimethyl-2-ethylbutyl
 group, 3,3-dimethyl-2-ethylbutyl group, 1,1-diethyl-2-
 methylpropyl group, 1-methyloctyl group, 2-methyloctyl
 20 group, 3-methyloctyl group,
 4-methyloctyl group, 5-methyloctyl group, 6-methyloctyl
 group, 7-methyloctyl group, 1-ethylheptyl group, 2-
 ethylheptyl group,
 3-ethylheptyl group, 4-ethylheptyl group, 5-ethylheptyl
 25 group, 1,1-dimethylheptyl group, 1,2-dimethylheptyl group,
 1,3-dimethylheptyl group, 1,4-dimethylheptyl group, 1,5-
 dimethylheptyl group, 1,6-dimethylheptyl group, 2,2-
 dimethylheptyl group, 2,3-dimethylheptyl group, 2,4-

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group, 3-nonenyl group, 4-nonenyl group, 5-nonenyl group, 6-nonenyl group, 7-nonenyl group, 2-decenyl group, 3-decenyl group, 4-decenyl group, 5-decenyl group, 6-decenyl group, 7-decenyl group, 8-decenyl group;

- 5 as well as branched alkenyl groups such as 1-methylethenyl group, 2-methyl-1-propenyl group, 2-methyl-2-propenyl group, 2-methyl-1-butenyl group, 3-methyl-2-butenyl group, 2-methyl-3-butenyl group, 2,3-dimethyl-1,3-butadienyl group, 3-ethyl-2-propenyl group, 4-methyl-3-propenyl group, 3-10 methyl-2,4-propadienyl group, 3,4-diethyl-2-hexenyl group, 4-methyl-3-hexenyl group, 2-methyl-4-hexenyl group, 3,5-dimethyl-2,4-hexadienyl group, 5-ethyl-3-methyl-2-heptenyl group, 5-methyl-3-heptenyl group, 4-n-propyl-4-heptenyl group, 3,6-dimethyl-5-heptenyl group, 5-ethyl-2,4-15 heptadienyl group, 2,6-dimethyl-2,5-heptadienyl group, 4-ethyl-3,5-heptadienyl group, 4,6-dimethyl-2-octenyl group, 5-ethyl-3-octenyl group, 3-ethyl-4-octenyl group, 3-ethyl-5-octenyl group, 3,4-dimethyl-6-octenyl group, 5-ethyl-2,4-octadienyl group, 3-methyl-2,5-octadienyl group, 5-ethyl-20 2,6-octadienyl group, 4-methyl-2,4,6-octatrienyl group, 5-methyl-2-nonenyl group, 6-methyl-3-nonenyl group, 7-methyl-4-nonenyl group, 3-methyl-5-nonenyl group, 4-methyl-6-nonenyl group, 3-methyl-7-nonenyl group, etc.

- 25 If Z is a straight-chained or branched alkynyl group having 2 - 10 carbon atoms that may optionally be substituted by a halogen atom, exemplary straight-chained or branched alkynyl groups having 2 - 10 carbon atoms include straight-chained alkynyl groups such as ethynyl



5-nonynyl group, 4-methyl-6-nonynyl group, 3-methyl-7-nonynyl group, etc.

If Z is $-O-R^d$, R^d is a hydrogen atom or a protective group for a hydroxyl group, and a hydrogen atom is

Typically, preferred examples of Z are a straight-chained or branched alkyl group having 1 - 10 carbon atoms that may optionally be substituted by a halogen atom, a hydroxyl group, and a straight-chained or branched alkyl group having 1 - 10 carbon atoms that is substituted by any one group selected from the group consisting of a cycloalkyl group having 3 - 6 carbon atoms, a hydroxyl group, a heterocyclic group and an optionally substituted phenyl group; straight-chained or branched alkyl groups having 3 - 10 carbon atoms that are substituted by a halogen atom are preferred and among these, straight-chained or branched alkyl groups having 3 - 8 carbon atoms that are substituted by a fluorine atom are particularly preferred, with 4,4,5,5,5-pentafluoropentyl group being most preferred. Considering peroral absorption, Z is preferably -COOH. Further considering peroral absorption, Z may preferably be a hydrogen atom if Q is Q¹⁷ where R⁷ is a hydrogen atom.

If Q is Q^{65} , Q^{66} , Q^{67} , Q^{68} , Q^{69} or Q^{70} , Z is preferably a



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morpholino group, pyrrolidinyl group, piperidino group, etc.

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5 5;

if p is 6, dimethylamino group and diethylamino group are preferred:

10 group, N-n-butyl-N-methylamino group, diethylamino group,
methylamino group, N-ethyl-N-methylamino group, N-methyl-N-
15 n-propylamino group, N-methyl-N-i-propylamino group, N-t-
butyl-N-methylamino group, n-propylamino group, n-
hexylamino group, i-pentylamino group, i-butylamino group,
2,2-dimethylpropylamino group, 1-ethylpropylamino group,
20 di-n-hexylamino group, amino group and n-pentylamino group
are preferred, with dimethylamino group, ethylamino group,
i-propylamino group, N-n-butyl-N-methylamino group,
diethylamino group, methylamino group, N-ethyl-N-methyl-

if p is 8, dimethylamino group, diethylamino group and N-n-butyl-N-methylamino group are preferred;

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if p is 13, amino group and n-pentylamino group are preferred;

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p in $-\text{Ph-O}-(\text{CH}_2)_p-\text{CO-NR}^8\text{Z}^1$ is preferably an integer of 1 - 7;
the group represented by $-\text{NR}^8\text{Z}^1$ in $-\text{Ph-O}-(\text{CH}_2)_p-\text{CO-NR}^8\text{Z}^1$ is

speaking further of that group,

if p is 3, amino group and n-pentylamino group are

preferred;

if p is 7, amino group and n-pentylamino group are preferred;

p in $-\text{Ph}-\text{O}-(\text{CH}_2)_p-\text{H}$ is preferably 1.

5 Referring further to the general formula (I), it is preferred that the dashed line in 4(5) position signifies a single bond or a double bond in combination with the solid line and X^2 signifies any one group selected from the group consisting of $-(\text{CH}_2)_p-\text{COOH}$ (p is an integer of at least 1),
 10 $-(\text{CH}_2)_p-\text{OH}$ (p has the same meaning as defined above), $-\text{Ph}-\text{O}-(\text{CH}_2)_p-\text{COOH}$ (Ph represents a phenylene group and p has the same meaning as defined above), $-(\text{CH}_2)_p-\text{CO}-\text{NR}^8\text{Z}^2$ (p has the same meaning as defined above, R^8 represents a hydrogen atom or a straight-chained or branched lower alkyl group
 15 having 1 - 6 carbon atoms, Z^2 represents a straight-chained or branched alkyl group having 1 - 10 carbon atoms that is substituted by any one group selected from the group consisting of a cycloalkyl group, a hydroxyl group, a carboxyl group, a heterocyclic group and a phenyl group, or
 20 $-\text{NR}^8\text{Z}^2$ may be such that N, R^8 and Z^2 combine together to form a hetero ring), $-(\text{CH}_2)_p-\text{Ph}-\text{O}-(\text{CH}_2)_q-\text{CO}-\text{NR}^8\text{Z}^3$ (Ph, p and R^8 have the same meanings as defined above, q represents an integer of at least 1, and Z^3 represents a hydrogen atom or a straight-chained or branched alkyl group having 1 - 10
 25 carbon atoms that may optionally be substituted by any one group selected from the group consisting of a cycloalkyl group, a hydroxyl group, a carboxyl group, a heterocyclic group and a phenyl group, or $-\text{NR}^8\text{Z}^3$ may be such that N, R^8

- and Z^3 combine together to form a hetero ring) and $-(CH_2)_p-CH(COOH)-(CH_2)_3-CF_2-CF_3$ (p has the same meaning as defined above), with p being more preferably an integer of 1 - 13;
 p in $-(CH_2)_p-COOH$ is preferably an integer of 5 - 13;
- 5 p in $-(CH_2)_p-OH$ is preferably an integer of 7 - 9;
 p in $-Ph-O-(CH_2)_p-COOH$ is preferably an integer of 1 - 7;
 p in $-(CH_2)_p-CO-NR^8Z^3$ is preferably an integer of 6 - 11;
 the group represented by $-NR^8Z^3$ in $-(CH_2)_p-CO-NR^8Z^3$ is preferably exemplified by, cyclohexylmethylamino group,
- 10 cyclopropylmethylamino group, 3-hydroxypropylamino group, t-butylbenzylamino group, 2,2-diphenylethylamino group, N-methyl-N-benzylamino group, phenylamino group, benzylamino group, 2-phenylethylamino group, piperidino group, pyrrolidinyl group and morpholino group, with N-methyl-N-
- 15 benzylamino group, benzylamino group, 2-phenylethylamino group, piperidino group, pyrrolidinyl group and morpholino group being more preferred, and piperidino group, pyrrolidinyl group and morpholino group being particularly preferred;
- 20 p in $-(CH_2)_p-Ph-O-(CH_2)_q-CO-NR^8Z^3$ is preferably 3;
 q in $-(CH_2)_p-Ph-O-(CH_2)_q-CO-NR^8Z^3$ is preferably 3 or 4;
 the group represented by $-NR^8Z^3$ in $-(CH_2)_p-Ph-O-(CH_2)_q-CO-NR^8Z^3$ is preferably exemplified by methylamino group, dimethylamino group and pyrrolidinyl group;
- 25 p in $-(CH_2)_p-CH(COOH)-(CH_2)_3-CF_2-CF_3$ is preferably 8;
 p in $-(CH_2)_p-Ph-O-(CH_2)_q-COOH$ is preferably 3;
 q in $-(CH_2)_p-Ph-O-(CH_2)_q-COOH$ is preferably 3 or 4.

Referring further to the general formula (I), it is



- being more preferably an integer of 3 - 13;
- p in $-(\text{CH}_2)_p\text{-COOH}$ is preferably an integer of 7 - 11;
- p in $-(\text{CH}_2)_p\text{-CH(COOH)-}(\text{CH}_2)_3\text{-CF}_2\text{-CF}_3$ is preferably 8;
- p in $-(\text{CH}_2)_p\text{-CH(COOMe)-}(\text{CH}_2)_3\text{-CF}_2\text{-CF}_3$ is preferably 8;
- 5 p in $-\text{O-}(\text{CH}_2)_p\text{-COOH}$ is preferably an integer of 5 - 13;
- p in $-\text{O-}(\text{CH}_2)_p\text{-CH(COOH)-}(\text{CH}_2)_3\text{-CF}_2\text{-CF}_3$ is preferably 8;
- p in $-(\text{CH}_2)_p\text{-S-}(\text{CH}_2)_3\text{-CF}_2\text{-CF}_3$ is preferably 10;
- p in $-(\text{CH}_2)_p\text{-SO-}(\text{CH}_2)_3\text{-CF}_2\text{-CF}_3$ is preferably 10;
- p in $-\text{O-}(\text{CH}_2)_p\text{-SO-}(\text{CH}_2)_3\text{-CF}_2\text{-CF}_3$ is preferably an integer of
- 10 5 - 13;
- p in $-\text{O-}(\text{CH}_2)_p\text{-SO}_2\text{-}(\text{CH}_2)_3\text{-CF}_2\text{-CF}_3$ is preferably an integer of
- 7 - 13;
- p in $-\text{Ph-O-}(\text{CH}_2)_p\text{-COOH}$ is preferably an integer of 3 - 7;
- p in $-(\text{CH}_2)_p\text{-CO-NR}^8\text{Z}^3$ is preferably an integer of 7 - 11;
- 15 the group represented by $-\text{NR}^8\text{Z}^3$ in $-(\text{CH}_2)_p\text{-CO-NR}^8\text{Z}^3$ is preferably exemplified by, amino group, n-pentylamino group, dimethylamino group, methylamino group, N-ethyl-N-methylamino group, N-methyl-N-n-propylamino group, diethylamino group, benzylamino group, N-n-butyl-N-
- 20 methylamino group, 2-hydroxyethylamino group, morpholino group and piperidino group;
- p in $-\text{Ph-O-}(\text{CH}_2)_p\text{-CO-NR}^8\text{Z}^3$ is preferably 7;
- the group represented by $-\text{NR}^8\text{Z}^3$ in $-\text{Ph-O-}(\text{CH}_2)_p\text{-CO-NR}^8\text{Z}^3$ is preferably exemplified by amino group and n-pentylamino
- 25 group;
- p in $-\text{O-}(\text{CH}_2)_p\text{-CO-NR}^8\text{Z}^3$ is preferably an integer of 5 - 13;
- the group represented by $-\text{NR}^8\text{Z}^3$ in $-\text{O-}(\text{CH}_2)_p\text{-CO-NR}^8\text{Z}^3$ is preferably exemplified by amino group and n-pentylamino

group.

Specifically, preferred examples of X^1 and X^2 are a hydrogen atom, 10-(4,4,5,5,5-pentafluoropentylsulfinyl)decyl group, 11-(4,4,5,5,5-pentafluoropentylsulfinyl)undecyl group, 12-(4,4,5,5,5-pentafluoropentylsulfinyl)dodecyl group, 10-(4,4,5,5,5-pentafluoropentylsulfonyl)decyl group, 11-(4,4,5,5,5-pentafluoropentylsulfonyl)undecyl group, 12-(4,4,5,5,5-pentafluoropentylsulfonyl)dodecyl group, 10-{N-(4,4,5,5,5-pentafluoropentyl)aminocarbonyl}decyl group, 11-{N-(4,4,5,5,5-pentafluoropentyl)aminocarbonyl}undecyl group, 9-{N-(5,5,6,6,6-pentafluorohexanoyl)amino}nonyl group, 10-{N-(5,5,6,6,6-pentafluorohexanoyl)amino}decyl group, 9-(4,4,5,5,5-pentafluoropentylsulfinyl)nonyloxy group, 10-(4,4,5,5,5-pentafluoropentylsulfinyl)decyloxy group, 11-(4,4,5,5,5-pentafluoropentylsulfinyl)undecyloxy group, 9-(4,4,5,5,5-pentafluoropentylsulfonyl)nonyloxy group, 10-(4,4,5,5,5-pentafluoropentylsulfonyl)decyloxy group, 11-(4,4,5,5,5-pentafluoropentylsulfonyl)undecyloxy group; 9-{N-(4,4,5,5,5-pentafluoropentyl)aminocarbonyl}nonyloxy group, 10-{N-(4,4,5,5,5-pentafluoropentyl)aminocarbonyl}decyloxy group, 8-{N-(5,5,6,6,6-pentafluorohexanoyl)amino}octyloxy group, 9-{N-(5,5,6,6,6-pentafluorohexanoyl)amino}nonyloxy group, 4-{8-(4,4,5,5,5-pentafluoropentylsulfinyl)octyloxy}phenyl group, 4-{9-(4,4,5,5,5-pentafluoropentylsulfinyl)nonyloxy}phenyl group, 4-{8-(4,4,5,5,5-pentafluoropentylsulfonyl)octyloxy}phenyl group, 4-{9-

(4,4,5,5,5-pentafluoropentylsulfonyl)nonyloxy}phenyl group,
 4-[8-{N-(4,4,5,5,5-pentafluoropentyl)aminocarbonyl}octyloxy]phenyl group, 4-[9-{N-(4,4,5,5,5-pentafluoropentyl)aminocarbonyl}nonyloxy]phenyl group, 4-[7-{N-(5,5,6,6,6-pentafluorohexanoyl)amino}heptyloxy]phenyl group, 4-[8-{N-(5,5,6,6,6-pentafluorohexanoyl)amino}octyloxy]phenyl group, 6-[4-{N-(4,4,5,5,5-pentafluoropentyl)aminocarbonyl}phenyl]hexyl group, 5-[4-{N-(4,4,5,5,5-pentafluoropentyl)aminocarbonyl}phenyl]pentyloxy group, tridecyloxy group, 11-carboxy-15,15,16,16,16-pentafluorohexadecyl group, 4-{{2-hydroxy-3-(4,4,5,5,5-pentafluoropentylsulfinylethyloxy)propyl}oxy}phenyl group, 4-hydroxy-9-(4,4,5,5,5-pentafluoropentylsulfinyl)nonyl group, 10-carboxy-14,14,15,15,15-pentafluoropentadecyloxy group, 9-carboxy-13,13,14,14,14-pentafluorotetradecyloxy group, 6-carboxy-10,10,11,11,11-pentafluoroundecyl group, 10-carboxy-14,14,15,15,15-pentafluoropentadecyl group, 14-carboxy-18,18,19,19,19-pentafluorononadecyl group, 9-carboxynonyloxy group, 6-carboxyhexyl group, 10-carboxydecyl group, 14-carboxytetradecyl group, 3-{4-(4-carboxybutyl)phenyl}propyl group, 3-{4-(4-carboxy-8,8,9,9,9-pentafluorononyl)phenyl}propyl group, 5-(4,4,5,5,5-pentafluoropentylsulfinyl)pentyl group, 9-(4,4,5,5,5-pentafluoropentylsulfinyl)nonyl group, 13-(4,4,5,5,5-pentafluoropentylsulfinyl)tridecyl group, 4-hydroxy-10-(4,4,5,5,5-pentafluoropentylsulfinyl)decyl group,

- 4-hydroxy-15,15,16,16,16-pentafluorohexadecyl group, 9-
 {N-(4,4,5,5,5-pentafluoropentyl)aminocarbonyl}nonyl group,
 and 8-{N-(5,5,6,6,6-pentafluorohexanoyl)amino}octyl group;
 5-carboxypentyl group, 7-carboxyheptyl group, 9-
 5 carboxynonyl group, 11-carboxyundecyl group, 13-
 carboxytridecyl group, 9-carboxy-13,13,14,14,14-
 pentafluorotetradecyl group, 9-methoxycarbonyl-
 13,13,14,14,14-pentafluorotetradecyl group, 5-
 carboxypentyloxy group, 7-carboxyheptyloxy group, 10-
 10 carboxydecyloxy group, 11-carboxyundecyloxy group, 13-
 carboxytridecyloxy group, 23-carboxytricosanyloxy group, 7-
 (N,N-dimethylaminocarbonyl)heptyl group, 7-(N-
 ethylaminocarbonyl)heptyl group, 7-{N-
 (cyclopropylmethyl)aminocarbonyl}heptyl group, 7-{N-
 15 (cyclohexylmethyl)aminocarbonyl}heptyl group, 7-(N-
 butylaminocarbonyl)heptyl group, 7-(N-
 isopropylaminocarbonyl)heptyl group, 7-(N-t-
 butylaminocarbonyl)heptyl group, 7-(N-
 cyclohexylaminocarbonyl)heptyl group, 7-{N-(3-
 20 hydroxypropyl)aminocarbonyl}heptyl group, 7-(N-methyl-N-
 butylaminocarbonyl)heptyl group, 7-(N,N-
 diethylaminocarbonyl)heptyl group, 7-
 (piperidinocarbonyl)heptyl group, 7-{N-(4-t-
 butylbenzyl)aminocarbonyl}heptyl group, 7-{N-(2,2-
 25 diphenylethyl)aminocarbonyl}heptyl group, 7-{N-(2-
 furylmethyl)aminocarbonyl}heptyl group, 7-(N-
 methylaminocarbonyl)heptyl group, 7-(N-methyl-N-
 ethylaminocarbonyl)heptyl group, 7-(N-methyl-N-

- propylaminocarbonyl)heptyl group, 7-(N-methyl-N-isopropylaminocarbonyl)heptyl group, 7-(N-methyl-N-benzylaminocarbonyl)heptyl group, 7-(1-pyrrolidinylcarbonyl)heptyl group, 7-
- 5 (morpholinocarbonyl)heptyl group, 7-(N-methyl-N-t-butylaminocarbonyl)heptyl group, 7-(N-cyclopropylaminocarbonyl)heptyl group, 6-(N,N-dimethylaminocarbonyl)hexyl group, 6-(N,N-diethylaminocarbonyl)hexyl group, 6-
- 10 (piperidinocarbonyl)hexyl group, 8-(N,N-dimethylaminocarbonyl)octyl group, 8-(N,N-diethylaminocarbonyl)octyl group, 8-(N-methyl-N-butylaminocarbonyl)octyl group, 8-(N-benzylaminocarbonyl)octyl group, 8-{N-(2-
- 15 hydroxyethyl)aminocarbonyl}octyl group, 8-(piperidinocarbonyl)octyl group, 9-(N,N-dimethylaminocarbonyl)nonyl group, 9-(N,N-diethylaminocarbonyl)nonyl group, 9-(1-pyrrolidinylcarbonyl)nonyl group, 9-(N-methyl-N-
- 20 ethylaminocarbonyl)nonyl group, 9-(N-methyl-N-butylaminocarbonyl)nonyl group, 9-(N-benzylaminocarbonyl)nonyl group, 9-(piperidinocarbonyl)nonyl group, 9-{N-(2-
- hydroxyethyl)aminocarbonyl}nonyl group, 9-(N-methyl-N-
- 25 propylaminocarbonyl)nonyl group, 9-(morpholinocarbonyl)nonyl group, 10-(N,N-dimethylaminocarbonyl)decyl group, 10-(N,N-diethylaminocarbonyl)decyl group, 10-(N-methyl-N-

- ethylaminocarbonyl)decyl group, 10-(N-methyl-N-propylaminocarbonyl)decyl group, 10-(N-methyl-N-butylaminocarbonyl)decyl group, 10-(morpholinocarbonyl)decyl group, 11-(N,N-
- 5 dimethylaminocarbonyl)undecyl group, 11-(N,N-diethylaminocarbonyl)undecyl group, 11-(piperidinocarbonyl)undecyl group, 11-(N-benzylaminocarbonyl)undecyl group, 11-(N-methyl-N-butylaminocarbonyl)undecyl group, 11-{N-(2-
- 10 hydroxyethyl)aminocarbonyl}undecyl group, 7-{N-(2-hydroxyethyl)aminocarbonyl}heptyl group, 7-(N-propylaminocarbonyl)heptyl group, 7-(N-hexylaminocarbonyl)heptyl group, 7-(N-isopentylaminocarbonyl)heptyl group, 7-(N-
- 15 isobutylaminocarbonyl)heptyl group, 7-(N-neopentylaminocarbonyl)heptyl group, 7-{N-(3-pentyl)aminocarbonyl}heptyl group, 7-(N,N-dihexylaminocarbonyl)heptyl group, 7-(N-phenylaminocarbonyl)heptyl group, 7-(N-
- 20 benzylaminocarbonyl)heptyl group, 7-{N-(2-phenylethyl)aminocarbonyl}heptyl group, 5-(aminocarbonyl)pentyl group, 5-(N-pentylaminocarbonyl)pentyl group, 7-(aminocarbonyl)heptyl group, 7-(N-pentylaminocarbonyl)heptyl group, 9-
- 25 (aminocarbonyl)nonyl group, 9-(N-pentylaminocarbonyl)nonyl group, 11-(aminocarbonyl)undecyl group, 11-(N-pentylaminocarbonyl)undecyl group, 13-(aminocarbonyl)tridecyl group, 13-(N-



4-{7-(4,4,5,5,5-pentafluoropentylsulfonyl)heptyloxy}phenyl group;

3-{3-(3-carboxypropoxy)phenyl}propyl group, 3-{3-(4-carboxybutoxy)phenyl}propyl group, 3-[3-{3-N-

5 methylaminocarbonyl}propoxy}phenyl}propyl group, 3-[3-{3-N,N-dimethylaminocarbonyl}propoxy}phenyl}propyl group, 3-[3-{3-(1-pyrrolidinylcarbonyl)propoxy}phenyl}propyl group, 3-[3-{4-N-methylaminocarbonyl}butoxy}phenyl}propyl group, 3-[3-{4-(N,N-dimethylaminocarbonyl)butoxy}phenyl}propyl

10 group, 3-[3-{4-(1-pyrrolidinylcarbonyl)butoxy}phenyl}propyl group;

5-(aminocarbonyl)pentyl group, 5-(N-pentylaminocarbonyl)pentyl group, 7-(aminocarbonyl)heptyl group, 7-(N-

15 pentylaminocarbonyl)heptyl group, 9-(aminocarbonyl)nonyl group, 9-(N-pentylaminocarbonyl)nonyl group, 11-(aminocarbonyl)undecyl group, 11-(N-pentylaminocarbonyl)undecyl group, 13-

20 (aminocarbonyl)tridecyl group, and 13-(N-pentylaminocarbonyl)tridecyl group. More preferred are 10-(4,4,5,5,5-pentafluoropentylsulfinyl)decyl group, 11-(4,4,5,5,5-pentafluoropentylsulfinyl)undecyl group, 11-(4,4,5,5,5-pentafluoropentylsulfonyl)undecyl group, 9-

25 (4,4,5,5,5-pentafluoropentylsulfinyl)nonyl group, 11-(4,4,5,5,5-pentafluoropentylsulfinyl)undecyl group, 9-(4,4,5,5,5-pentafluoropentylsulfonyl)nonyl group, 11-(4,4,5,5,5-pentafluoropentylsulfonyl)undecyl group, 9-

- carboxy-13,13,14,14,14-pentafluorotetradecyloxy group, 9-carboxynonyloxy group, 5-(4,4,5,5,5-pentafluoropentylsulfinyl)pentyl group, 9-(4,4,5,5,5-pentafluoropentylsulfinyl)nonyl group;
- 5 5-carboxypentyl group, 7-carboxyheptyl group, 9-carboxynonyl group, 11-carboxyundecyl group, 13-carboxytridecyl group, 9-carboxy-13,13,14,14,14-pentafluorotetradecyl group, 9-methoxycarbonyl-13,13,14,14,14-pentafluorotetradecyl group, 5-
- 10 carboxypentyloxy group, 7-carboxyheptyloxy group, 10-carboxydecyloxy group, 11-carboxyundecyloxy group, 13-carboxytridecyloxy group, 23-carboxytricosanyloxy group, 7-(N,N-dimethylaminocarbonyl)heptyl group, 7-(N-ethylaminocarbonyl)heptyl group, 7-{N-
- 15 (cyclopropylmethyl)aminocarbonyl}heptyl group, 7-{N-(cyclohexylmethyl)aminocarbonyl}heptyl group, 7-(N-butylaminocarbonyl)heptyl group, 7-(N-isopropylaminocarbonyl)heptyl group, 7-(N-t-butylaminocarbonyl)heptyl group, 7-(N-
- 20 cyclohexylaminocarbonyl)heptyl group, 7-{N-(3-hydroxypropyl)aminocarbonyl}heptyl group, 7-(N-methyl-N-butylaminocarbonyl)heptyl group, 7-(N,N-diethylaminocarbonyl)heptyl group, 7-
- (piperidinocarbonyl)heptyl group, 7-{N-(4-t-
- 25 butylbenzyl)aminocarbonyl}heptyl group, 7-{N-(2,2-diphenylethyl)aminocarbonyl}heptyl group, 7-{N-(2-furylmethyl)aminocarbonyl}heptyl group, 7-(N-methylaminocarbonyl)heptyl group, 7-(N-methyl-N-

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- diethylaminocarbonyl)decyl group, 10-(N-methyl-N-ethylaminocarbonyl)decyl group, 10-(N-methyl-N-propylaminocarbonyl)decyl group, 10-(N-methyl-N-butylaminocarbonyl)decyl group, 10-
- 5 (morpholinocarbonyl)decyl group, 11-(N,N-dimethylaminocarbonyl)undecyl group, 11-(N,N-diethylaminocarbonyl)undecyl group, 11-(piperidinocarbonyl)undecyl group, 11-(N-benzylaminocarbonyl)undecyl group, 11-(N-methyl-N-
- 10 butylaminocarbonyl)undecyl group, 11-{N-(2-hydroxyethyl)aminocarbonyl}undecyl group, 7-{N-(2-hydroxyethyl)aminocarbonyl}heptyl group, 7-(N-propylaminocarbonyl)heptyl group, 7-(N-hexylaminocarbonyl)heptyl group, 7-(N-
- 15 isopentylaminocarbonyl)heptyl group, 7-(N-isobutylaminocarbonyl)heptyl group, 7-(N-neopentylaminocarbonyl)heptyl group, 7-{N-(3-pentyl)aminocarbonyl}heptyl group, 7-(N,N-dihexylaminocarbonyl)heptyl group, 7-(N-
- 20 phenylaminocarbonyl)heptyl group, 7-(N-benzylaminocarbonyl)heptyl group, 7-{N-(2-phenylethyl)aminocarbonyl}heptyl group, 5-(aminocarbonyl)pentyl group, 5-(N-pentylaminocarbonyl)pentyl group, 7-(aminocarbonyl)heptyl
- 25 group, 7-(N-pentylaminocarbonyl)heptyl group, 9-(aminocarbonyl)nonyl group, 9-(N-pentylaminocarbonyl)nonyl group, 11-(aminocarbonyl)undecyl group, 11-(N-pentylaminocarbonyl)undecyl group, 13-

(aminocarbonyl)tridecyl group, 13-(N-pentylaminocarbonyl)tridecyl group, 8-(N-methyl-N-ethylaminocarbonyl)octyl group, 8-(N-methyl-N-propylaminocarbonyl)octyl group, 8-

5 (morpholinocarbonyl)octyl group, 8-(N-methylaminocarbonyl)octyl group, 10-(4,4,5,5,5-pentafluoropentylsulfanyl)decyl group, 7-hydroxyheptyl group, 8-hydroxyoctyl group, 9-hydroxynonyl group, 7-(4,4,5,5,5-pentafluoropentylsulfinyl)heptyl group, 7-

10 (4,4,5,5,5-pentafluoropentylsulfonyl)heptyl group, 9-(4,4,5,5,5-pentafluoropentylsulfonyl)nonyl group, 13-(4,4,5,5,5-pentafluoropentylsulfonyl)tridecyl group; 4-(carboxymethoxy)phenyl group, 4-(3-carboxypropoxy)phenyl group, 4-(7-carboxyheptyloxy)phenyl group, 4-

15 (carbamoylmethoxy)phenyl group, 4-(3-carbamoylpropoxy)phenyl group, 4-(7-carbamoylheptyloxy)phenyl group, 4-(3-N-pentylcarbamoylpropoxy)phenyl group, 4-(7-N-pentylcarbamoylheptyloxy)phenyl group, 4-methoxyphenyl

20 group;

5-(4,4,5,5,5-pentafluoropentylsulfinyl)pentylloxy group, 7-(4,4,5,5,5-pentafluoropentylsulfinyl)heptyloxy group, 13-(4,4,5,5,5-pentafluoropentylsulfinyl)tridecyloxy group; 7-(4,4,5,5,5-pentafluoropentylsulfonyl)heptyloxy group, 13-

25 (4,4,5,5,5-pentafluoropentylsulfonyl)tridecyloxy group; 4-{5-(4,4,5,5,5-pentafluoropentylsulfinyl)pentylloxy}phenyl group, 4-{7-(4,4,5,5,5-pentafluoropentylsulfinyl)heptyloxy}phenyl group, 4-{5-

(4,4,5,5,5-pentafluoropentylsulfonyl)pentylloxy}phenyl group,
 4-{7-(4,4,5,5,5-pentafluoropentylsulfonyl)heptyloxy group;
 3-{3-(3-carboxypropoxy)phenyl}propyl group, 3-{3-(4-
 carboxybutoxy)phenyl}propyl group, 3-[3-{3-N-
 5 methylaminocarbonyl}propoxy}phenyl]propyl group, 3-[3-{3-
 N,N-dimethylaminocarbonyl}propoxy}phenyl]propyl group, 3-
 [3-{3-(1-pyrrolidinylcarbonyl)propoxy}phenyl]propyl group,
 3-[3-{4-(N-methylaminocarbonyl)butoxy}phenyl]propyl group,
 3-[3-{4-(N,N-dimethylaminocarbonyl)butoxy}phenyl]propyl
 10 group, and 3-[3-{4-(1-
 pyrrolidinylcarbonyl)butoxy}phenyl]propyl group;
 as well as 5-(aminocarbonyl)pentylloxy group, 5-(N-
 pentylaminocarbonyl)pentylloxy group, 7-
 (aminocarbonyl)heptyloxy group, 7-(N-
 15 pentylaminocarbonyl)heptyloxy group, 9-
 (aminocarbonyl)nonyloxy group, 9-(N-
 pentylaminocarbonyl)nonyloxy group, 11-
 (aminocarbonyl)undecyloxy group, 11-(N-
 pentylaminocarbonyl)undecyloxy group, 13-
 20 (aminocarbonyl)tridecyloxy group, and 13-(N-
 pentylaminocarbonyl)tridecyloxy group.

Particularly preferred are 7-(N,N-
 dimethylaminocarbonyl)heptyl group, 7-(N-
 ethylaminocarbonyl)heptyl group, 7-(N-
 25 isopropylaminocarbonyl)heptyl group, 7-(N-methyl-N-
 butylaminocarbonyl)heptyl group, 7-(N,N-
 diethylaminocarbonyl)heptyl group, 7-
 (piperidinocarbonyl)heptyl group, 7-{N-(2-

furylmethyl)aminocarbonyl}heptyl group, 7-(N-methylaminocarbonyl)heptyl group, 7-(N-methyl-N-ethylaminocarbonyl)heptyl group, 7-(N-methyl-N-propylaminocarbonyl)heptyl group, 7-(N-methyl-N-isopropylaminocarbonyl)heptyl group, 7-(N-methyl-N-benzylaminocarbonyl)heptyl group, 7-(1-pyrrolidinylcarbonyl)heptyl group, 7-(morpholinocarbonyl)heptyl group, 9-(N,N-dimethylaminocarbonyl)nonyl group, 9-(N,N-diethylaminocarbonyl)nonyl group, 9-(N-methyl-N-butylaminocarbonyl)nonyl group, 9-(N-methyl-N-propylaminocarbonyl)nonyl group, 9-(morpholinocarbonyl)nonyl group, 10-(N,N-dimethylaminocarbonyl)decyl group, 7-{N-(2-hydroxyethyl)aminocarbonyl}heptyl group, 7-(N-propylaminocarbonyl)heptyl group, 7-(N-benzylaminocarbonyl)heptyl group, 7-{N-(2-phenylethyl)aminocarbonyl}heptyl group, 3-[3-{3-N-methylaminocarbonyl}propoxy}phenyl]propyl group, 3-[3-{3-(N,N-dimethylaminocarbonyl)propoxy}phenyl]propyl group, and 3-[3-{4-(1-pyrrolidinylcarbonyl)butoxy}phenyl]propyl group.

It should however be noted that X^1 and X^2 are not a hydrogen atom at the same time. Particularly preferred cases are such that X^1 is a hydrogen atom and X^2 is any one of the groups listed above except a hydrogen atom, as well as where X^1 is any one of the groups listed above except a hydrogen atom and X^2 is a hydrogen atom.

Preferred examples of the compound represented by the

17 β -hydroxy-11 β -(9-(4,4,5,5,5-

17 β -hydroxy-11 β -{11-(4,4,5,5,5-

17 β -hydroxy-11 β -(9-(4,4,5,5,5-

10 17 β -hydroxy-11 β -{11-(4,4,5,5,5-

17 β -hydroxy-11 β -(9-carboxy-13,13,14,14,14-

17 β -hydroxy-11 β -(9-carboxynonyloxy)-5 α -androstan-3-one;

pentafluoropentylsulfinyl)dodecyl}-5 α -androstan-3-one;

17 β -hydroxy-11 β -{10-(4,4,5,5,5-

pentafluoropentylsulfonyl)decyl}-5 α -androstan-3-one;

17 β -hydroxy-11 β -{11-(4,4,5,5,5-

20 pentafluoropentylsulfonyl)undecyl}-5 α -androstan-3-one;

17 β -hydroxy-11 β -{12-(4,4,5,5,5-

pentafluoropentylsulfonyl)dodecyl}-5 α -androstan-3-one;

17 β -hydroxy-11 β -[10-{N-(4,4,5,5,5-

pentafluoropentyl)aminocarbonyl}decyl]-5 α -androstan-3-one;

25 17 β -hydroxy-11 β -[11-{N-(4,4,5,5,5-

pentafluoropentyl)aminocarbonyl}undecyl]-5 α -androstan-3-one;

17 β -hydroxy-11 β -[9-{N-(5,5,6,6,6-

17 β -hydroxy-11 β -[4-{8-(4,4,5,5,5-

17 β -hydroxy-11 β -[4-{9-(4,4,5,5,5-

10 17 β -hydroxy-11 β -(4-[8-{N-(4,4,5,5,5-

17 β -hydroxy-11 β -(4-[9-{N-(4,4,5,5,5-

17 β -hydroxy-11 β -(4-[7-{N-(5,5,6,6,6-

17 β -hydroxy-11 β -(4-[8-{N-(5,5,6,6,6-

17 β -hydroxy-11 β -(6-[4-{N-(4,4,5,5,5-

25 17 β -hydroxy-11 β -(5-[4-{N-(4,4,5,5,5-

17 β -hydroxy-11 β -tridecyloxy-5 α -androstan-3-one;

- 17 β -hydroxy-11 β -(11-carboxy-15,15,16,16,16-pentafluorohexadecyl)-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[4-{{2-hydroxy-3-(4,4,5,5,5-pentafluoropentylsulfinylethyloxy)propyl}oxy}phenyl]-5 α -
- 5 androstan-3-one;
- 17 β -hydroxy-11 β -{4-hydroxy-9-(4,4,5,5,5-pentafluoropentylsulfinyl)nonyl}-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -(10-carboxy-14,14,15,15,15-pentafluoropentadecyloxy)-5 α -androstan-3-one;
- 10 17 β -hydroxy-11 β -(9-carboxy-13,13,14,14,14-pentafluorotetradecyloxy)-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -(6-carboxy-10,10,11,11,11-pentafluoroundecyl)-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -(10-carboxy-14,14,15,15,15-pentafluoropentadecyl)-5 α -androstan-3-one;
- 15 17 β -hydroxy-11 β -(14-carboxy-18,18,19,19,19-pentafluorononadecyl)-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -(9-carboxynonyloxy)-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -(6-carboxyhexyl)-5 α -androstan-3-one;
- 20 17 β -hydroxy-11 β -(10-carboxydecyl)-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -(14-carboxytetradecyl)-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[3-{4-(4-carboxybutyl)phenyl}propyl]-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[3-{4-(4-carboxy-8,8,9,9,9-pentafluorononyl)phenyl}propyl]-5 α -androstan-3-one;
- 25 17 β -hydroxy-11 β -{5-(4,4,5,5,5-pentafluoropentylsulfinyl)pentyl}-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -{9-(4,4,5,5,5-

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- pentafluorotetradecyl)-5 α -androstan-3-one;
 17 β -hydroxy-11 β -(9-methoxycarbonyl-13,13,14,14,14-pentafluorotetradecyl)-5 α -androstan-3-one;
 17 β -hydroxy-11 β -(5-carboxypentyloxy)-5 α -androstan-3-one;
 5 17 β -hydroxy-11 β -(7-carboxyheptyloxy)-5 α -androstan-3-one;
 17 β -hydroxy-11 β -(10-carboxydecyloxy)-5 α -androstan-3-one;
 17 β -hydroxy-11 β -(11-carboxyundecyloxy)-5 α -androstan-3-one;
 17 β -hydroxy-11 β -(13-carboxytridecyloxy)-5 α -androstan-3-one;
 17 β -hydroxy-11 β -(23-carboxytricosanyloxy)-5 α -androstan-3-
 10 one;
 17 β -hydroxy-7 α -{7-(N,N-dimethylaminocarbonyl)heptyl}-5 α -androstan-3-one;
 17 β -hydroxy-7 α -{7-(N-ethylaminocarbonyl)heptyl}-5 α -androstan-3-one;
 15 17 β -hydroxy-7 α -[7-{N-(cyclopropylmethyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-{N-(cyclohexylmethyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
 20 17 β -hydroxy-7 α -[7-(N-butylaminocarbonyl)heptyl]-5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-(N-(isopropylaminocarbonyl)heptyl)-5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-(N-t-butylaminocarbonyl)heptyl]-5 α -
 25 androstan-3-one;
 17 β -hydroxy-7 α -[7-(N-cyclohexylaminocarbonyl)heptyl]-5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-{N-(3-

- hydroxypropyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-(N-methyl-N-butylaminocarbonyl)heptyl]-
 5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-(N,N-diethylaminocarbonyl)heptyl]-5 α -
 5 androstan-3-one;
 17 β -hydroxy-7 α -[7-(piperidinocarbonyl)heptyl]-5 α -androstan-
 3-one;
 17 β -hydroxy-7 α -[7-{N-(4-t-
 butylbenzyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
 10 17 β -hydroxy-7 α -[7-{N-(2,2-
 diphenylethyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-{N-(2-furylmethyl)aminocarbonyl}heptyl]-
 5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-{7-(N-methylaminocarbonyl)heptyl]-5 α -
 15 androstan-3-one;
 17 β -hydroxy-7 α -[7-(N-methyl-N-ethylaminocarbonyl)heptyl]-
 5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-(N-methyl-N-propylaminocarbonyl)heptyl]-
 5 α -androstan-3-one;
 20 17 β -hydroxy-7 α -[7-(N-methyl-N-
 isopropylaminocarbonyl)heptyl]-5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-(N-methyl-N-benzylaminocarbonyl)heptyl]-
 5 α -androstan-3-one;
 17 β -hydroxy-7 α -[7-(1-pyrrolidinylcarbonyl)heptyl]-5 α -
 25 androstan-3-one;
 17 β -hydroxy-7 α -[7-(morpholinocarbonyl)heptyl]-5 α -androstan-
 3-one;
 17 β -hydroxy-7 α -[7-(N-methyl-N-t-butylaminocarbonyl)heptyl]-

[illegible]

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- androstan-3-one;
- 17 β -hydroxy-7 α -[9-(N-methyl-N-butylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(N-benzylaminocarbonyl)nonyl]-5 α -
- 5 androstan-3-one;
- 17 β -hydroxy-7 α -[9-(piperidinocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-{N-(2-hydroxyethyl)aminocarbonyl)nonyl]-5 α -androstan-3-one;
- 10 17 β -hydroxy-7 α -[9-(N-methyl-N-propylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(morpholinocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[10-(N,N-dimethylaminocarbonyl)decyl]-5 α -
- 15 androstan-3-one;
- 17 β -hydroxy-7 α -[10-(N,N-diethylaminocarbonyl)decyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[10-(N-methyl-N-ethylaminocarbonyl)decyl]-5 α -androstan-3-one;
- 20 17 β -hydroxy-7 α -[10-N-methyl-N-propylaminocarbonyl)decyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[10-(N-methyl-N-butylaminocarbonyl)decyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[10-(morpholinocarbonyl)decyl]-5 α -androstan-
- 25 3-one;
- 17 β -hydroxy-7 α -[11-(N,N-dimethylaminocarbonyl)undecyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[11-(N,N-diethylaminocarbonyl)undecyl]-5 α -

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17 β -hydroxy-11 β -(7-carboxyheptyl)-5 α -androstan-3-one;

17 β -hydroxy-11 β -(9-carboxynonyl)-5 α -androstan-3-one;

17 β -hydroxy-7 α -[5-(aminocarbonyl)pentyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[7-(aminocarbonyl)heptyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[9-(aminocarbonyl)nonyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[9-(N-pentylaminocarbonyl)nonyl]-5 α -

17 β -hydroxy-11 β -[9-(N-pentylaminocarbonyl)nonyl]-5
androstan-3-one;

17 β -hydroxy-11 β -[11-(aminocarbonyl)undecyl]-5 α -androstan-3-one;

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- 17 β -hydroxy-11 β -[11-(N-pentylaminocarbonyl)undecyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[13-(aminocarbonyl)tridecyl]-5 α -androstan-3-one;
- 5 17 β -hydroxy-7 α -[13-(N-pentylaminocarbonyl)tridecyl]-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -{7-(N,N-dimethylaminocarbonyl)heptyl}-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[7-{7-(N-methylaminocarbonyl)heptyl}-5 α -androstan-3-one;
- 10 17 β -hydroxy-11 β -[7-(N-methyl-N-ethylaminocarbonyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[7-(N-methyl-N-propylaminocarbonyl)heptyl]-5 α -androstan-3-one;
- 15 17 β -hydroxy-11 β -[7-(morpholinocarbonyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[8-(N,N-dimethylaminocarbonyl)octyl]-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[8-(N-methylaminocarbonyl)octyl]-5 α -androstan-3-one;
- 20 17 β -hydroxy-11 β -[8-(N-methyl-N-ethylaminocarbonyl)octyl]-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[8-(N-methyl-N-propylaminocarbonyl)octyl]-5 α -androstan-3-one;
- 25 17 β -hydroxy-11 β -[8-(morpholinocarbonyl)octyl]-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[9-(N,N-dimethylaminocarbonyl)nonyl]-5 α -androstan-3-one;

- 17 β -hydroxy-11 β -[9-(N,N-diethylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[9-(N-methyl-N-butylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 5 17 β -hydroxy-11 β -[9-(N-benzylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[9-(piperidinocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[9-{N-(2-hydroxyethyl)aminocarbonyl}nonyl]-5 α -androstan-3-one;
- 10 17 β -hydroxy-11 β -[10-(4,4,5,5,5-pentafluoropentylsulfanyl)decyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -(7-hydroxyheptyl)-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -(8-hydroxyoctyl)-5 α -androstan-3-one;
- 15 17 β -hydroxy-7 α -(9-hydroxynonyl)-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(4,4,5,5,5-pentafluoropentylsulfinyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[13-(4,4,5,5,5-pentafluoropentylsulfinyl)tridecyl]-5 α -androstan-3-one;
- 20 17 β -hydroxy-7 α -[7-(4,4,5,5,5-pentafluoropentylsulfonyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(4,4,5,5,5-pentafluoropentylsulfonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[13-(4,4,5,5,5-pentafluoropentylsulfonyl)tridecyl]-5 α -androstan-3-one;
- 25 17 β -hydroxy-7 α -[4-(carboxymethoxy)phenyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[4-(3-carboxypropoxy)phenyl]-5 α -androstan-3-

17 β -hydroxy-11 β -[4-(3-carboxypropoxy)phenyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[4-(7-carboxyheptyloxy)phenyl]-5 α -androstan-3-one;

17 β -hydroxy-11 β -[4-(7-carboxyheptyloxy)phenyl]-5 α -
androstan-3-one;

17 β -hydroxy-7 α -[4-(carbamoylmethoxy)phenyl]-5 α -androstan-3-one:

10 17 β -hydroxy-7 α -[4-(carbamoylmethoxy)phenyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[4-(3-carbamoylpropoxy)phenyl]-5 α -androstan-3-one;

17 β -hydroxy-11 β -[4-(3-carbamoylpropoxy)phenyl]-5 α -
15 androstan-3-one:

17 β -hydroxy-7 α -[4-(7-carbamoylheptyloxy)phenyl]-5 α -
androstane-3-one;

17 β -hydroxy-11 β -[4-(7-carbamoylheptyloxy)phenyl]-5 α -
androstan-3-one;

20 17 β -hydroxy-7 α -[4-(3-N-pentylcarbamoylpropoxy)phenyl]-5 α -
androstan-3-one;

17 β -hydroxy-11 β -[4-(3-N-pentylcarbamoylpropoxy)phenyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[4-(7-N-pentylcarbamoylheptyloxy)phenyl]-5 α -
25 androstan-3-one;

17 β -hydroxy-11 β -[4-(7-N-pentylcarbamoylheptyloxy)phenyl]-
5 α -androstan-3-one;

17 β -hydroxy-7 α -[4-methoxyphenyl]-5 α -androstan-3-one;

5

$$17\beta\text{-hydroxy-}7\alpha\text{-[3-[3-\{3-(1-$$

10

17 β -hydroxy-7 α -[3-[3-{4-(N,N-

15

17 β -hydroxy-11 β -[5-(aminocarbonyl)pentyl]oxy]-5 α -androstan-

20

17 β -hydroxy-11 β -[7-(aminocarbonyl)heptyloxy]-5 α -androsterane-

25

17 β -hydroxy-11 β -[9-(aminocarbonyl)nonyloxy]-5 α -androsterane-

17 β -hydroxy-11 β -[9-(N-pentylaminocarbonyl)nonyloxy]-5 α -

- androstan-3-one;
 17 β -hydroxy-11 β -[11-(aminocarbonyl)undecyloxy]-5 α -
 androstan-one;
 17 β -hydroxy-11 β -[11-(N-pentylaminocarbonyl)undecyloxy]-5 α -
 5 androstan-3-one;
 17 β -hydroxy-11 β -[13-(aminocarbonyl)tridecyloxy]-5 α -
 androstan-3-one;
 17 β -hydroxy-11 β -[13-(N-pentylaminocarbonyl)tridecyloxy]-5 α -
 androstan-3-one;
 10 more preferred are the following:
 17 β -hydroxy-11 β -{10-(4,4,5,5,5-
 pentafluoropentylsulfinyl)decyl}-5 α -androstan-3-one;
 17 β -hydroxy-11 β -{9-(4,4,5,5,5-
 pentafluoropentylsulfinyl)nonyloxy}-5 α -androstan-3-one;
 15 17 β -hydroxy-11 β -{11-(4,4,5,5,5-
 pentafluoropentylsulfinyl)undecyloxy}-5 α -androstan-3-one;
 17 β -hydroxy-11 β -{9-(4,4,5,5,5-
 pentafluoropentylsulfonyl)nonyloxy}-5 α -androstan-3-one;
 17 β -hydroxy-11 β -{11-(4,4,5,5,5-
 20 pentafluoropentylsulfonyl)undecyloxy}-5 α -androstan-3-one;
 17 β -hydroxy-11 β -(9-carboxy-13,13,14,14,14-
 pentafluorotetradecyloxy)-5 α -androstan-3-one;
 17 β -hydroxy-11 β -(9-carboxynonyloxy)-5 α -androstan-3-one;
 17 β -hydroxy-7 α -{11-(4,4,5,5,5-
 25 pentafluoropentylsulfinyl)undecyl}-5 α -androstan-3-one;
 17 β -hydroxy-7 α -{11-(4,4,5,5,5-
 pentafluoropentylsulfonyl)undecyl}-5 α -androstan-3-one;
 17 β -hydroxy-7 α -{5-(4,4,5,5,5-



- 17 β -hydroxy-7 α -[7-{N-(cyclohexylmethyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[7-(N-butylaminocarbonyl)heptyl]-5 α -androstan-3-one;
- 5 17 β -hydroxy-7 α -[7-(N-(isopropylaminocarbonyl)heptyl)-5 α -androstan-3-one;
17 β -hydroxy-7 α -[7-(N-t-butylaminocarbonyl)heptyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[7-(N-cyclohexylaminocarbonyl)heptyl]-5 α -
- 10 androstan-3-one;
17 β -hydroxy-7 α -[7-{N-(3-hydroxypropyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[7-(N-methyl-N-butylaminocarbonyl)heptyl]-5 α -androstan-3-one;
- 15 17 β -hydroxy-7 α -[7-(N,N-diethylaminocarbonyl)heptyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[7-(piperidinocarbonyl)heptyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[7-{N-(4-t-
- 20 butylbenzyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[7-{N-(2,2-diphenylethyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[7-{N-(2-furylmethyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
- 25 17 β -hydroxy-7 α -[7-{7-(N-methylaminocarbonyl)heptyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[7-(N-methyl-N-ethylaminocarbonyl)heptyl]-5 α -androstan-3-one;

- 17 β -hydroxy-7 α -[7-(N-methyl-N-propylaminocarbonyl)heptyl]-
5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(N-methyl-N-
isopropylaminocarbonyl)heptyl]-5 α -androstan-3-one;
- 5 17 β -hydroxy-7 α -[7-(N-methyl-N-benzylaminocarbonyl)heptyl]-
5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(1-pyrrolidinylcarbonyl)heptyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-7 α -[7-(morpholinocarbonyl)heptyl]-5 α -androstan-
10 3-one;
- 17 β -hydroxy-7 α -[7-(N-methyl-N-t-butylaminocarbonyl)heptyl]-
5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(N-cyclopropylaminocarbonyl)heptyl]-5 α -
androstan-3-one;
- 15 17 β -hydroxy-7 α -[6-(N,N-dimethylaminocarbonyl)hexyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-7 α -[6-(N,N-diethylaminocarbonyl)hexyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-7 α -[6-(piperidinocarbonyl)hexyl]-5 α -androstan-
20 3-one;
- 17 β -hydroxy-7 α -[8-(N,N-dimethylaminocarbonyl)octyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-7 α -[8-(N,N-diethylaminocarbonyl)octyl]-5 α -
androstan-3-one;
- 25 17 β -hydroxy-7 α -[8-(N-methyl-N-butylaminocarbonyl)octyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-7 α -[8-(N-benzylaminocarbonyl)octyl]-5 α -
androstan-3-one;

- 17 β -hydroxy-7 α -[8-{N-(2-hydroxyethyl)aminocarbonyl}octyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[8-(piperidinocarbonyl)octyl]-5 α -androstan-3-one;
- 5 17 β -hydroxy-7 α -[9-(N,N-dimethylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(N,N-diethylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(1-pyrrolidinylcarbonyl)nonyl]-5 α -
- 10 androstan-3-one;
- 17 β -hydroxy-7 α -[9-(N-methyl-N-ethylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(N-methyl-N-butylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 15 17 β -hydroxy-7 α -[9-(N-benzylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(piperidinocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-{N-(2-hydroxyethyl)aminocarbonyl}nonyl]-
- 20 5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(N-methyl-N-propylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(morpholinocarbonyl)nonyl]-5 α -androstan-3-one;
- 25 17 β -hydroxy-7 α -[10-(N,N-dimethylaminocarbonyl)decyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[10-(N,N-diethylaminocarbonyl)decyl]-5 α -androstan-3-one;

- 17 β -hydroxy-7 α -[10-(N-methyl-N-ethylaminocarbonyl)decyl]-
5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[10-N-methyl-N-propylaminocarbonyl)decyl]-
5 α -androstan-3-one;
- 5 17 β -hydroxy-7 α -[10-(N-methyl-N-butylaminocarbonyl)decyl]-
5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[10-(morpholinocarbonyl)decyl]-5 α -androstan-
3-one;
- 17 β -hydroxy-7 α -[11-(N,N-dimethylaminocarbonyl)undecyl]-5 α -
10 androstan-3-one;
- 17 β -hydroxy-7 α -[11-(N,N-diethylaminocarbonyl)undecyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-7 α -[11-(piperidinocarbonyl)undecyl]-5 α -
androstan-3-one;
- 15 17 β -hydroxy-7 α -[11-(N-benzylaminocarbonyl)undecyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-7 α -[11-(N-methyl-N-butylaminocarbonyl)undecyl]-
5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[11-{N-(2-
20 hydroxyethyl)aminocarbonyl}undecyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-{N-(2-hydroxyethyl)aminocarbonyl}heptyl]-
5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(N-propylaminocarbonyl)heptyl]-5 α -
androstan-3-one;
- 25 17 β -hydroxy-7 α -[7-(N-hexylaminocarbonyl)heptyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-7 α -[7-(N-isopentylaminocarbonyl)heptyl]-5 α -
androstan-3-one;

17 β -hydroxy-7 α -[7-(N-neopentylaminocarbonyl)heptyl]-5 α -
androstan-3-one;

17 β -hydroxy-7 α -[7-(N,N-dihexylaminocarbonyl)heptyl]-5 α -androstane-3-one;

17 β -hydroxy-7 α -[7-(N-benzylaminocarbonyl)heptyl]-5 α -
androstan-3-one;

17β-hydroxy-7α-[7-{N-(2-phenylethyl)aminocarbonyl}heptyl]-
5α-androstan-3-one;

15 17 β -hydroxy-11 β -(7-carboxyheptyl)-5 α -androstan-3-one;

17 β -hydroxy-11 β -(8-carboxyoctyl)-5 α -androstan-3-one;

17 β -hydroxy-11 β -(9-carboxynonyl)-5 α -androstan-3-one;

17 β -hydroxy-11 β -(11-carboxyundecyl)-5 α -androstan-3-one;

17 β -hydroxy-7 α -[5-(aminocarbonyl)pentyl]-5 α -androstan-3-
20 one;

17 β -hydroxy-7 α -[5-(N-pentylaminocarbonyl)pentyl]-5 α -
androstan-3-one:

17 β -hydroxy-7 α -[7-(aminocarbonyl)heptyl]-5 α -androstan-3-one;

25 17 β -hydroxy-7 α -[7-(N-pentylaminocarbonyl)heptyl]-5 α -
androstan-3-one:

17 β -hydroxy-7 α -[9-(aminocarbonyl)nonyl]-5 α -androstan-3-one;

17 β -hydroxy-11 β -[9-(aminocarbonyl)nonyl]-5 α -androstan-3-

5

one -

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androstan-3-one.

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androstan-3-one.

androstan-3-one.

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5 α -androstane-3-one:

25

androstan-3-one.

17 β -hydroxy-11 β -[8-(N,N-dimethylaminocarbonyl)octyl]-5 α -

- androstan-3-one;
- 17 β -hydroxy-11 β -[8-(N-methylaminocarbonyl)octyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-11 β -[8-(N-methyl-N-ethylaminocarbonyl)octyl]-
5 5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[8-(N-methyl-N-propylaminocarbonyl)octyl]-
5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[8-(morpholinocarbonyl)octyl]-5 α -androstan-
3-one;
- 10 17 β -hydroxy-11 β -[9-(N,N-dimethylaminocarbonyl)nonyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-11 β -[9-(N,N-diethylaminocarbonyl)nonyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-11 β -[9-(N-methyl-N-butylaminocarbonyl)nonyl]-
15 5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[9-(N-benzylaminocarbonyl)nonyl]-5 α -
androstan-3-one;
- 17 β -hydroxy-11 β -[9-(piperidinocarbonyl)nonyl]-5 α -androstan-
3-one;
- 20 17 β -hydroxy-11 β -[9-{N-(2-hydroxyethyl)aminocarbonyl}nonyl]-
5 α -androstan-3-one;
- 17 β -hydroxy-11 β -[10-(4,4,5,5,5-
pentafluoropentylsulfanyl)decyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -(7-hydroxyheptyl)-5 α -androstan-3-one;
- 25 17 β -hydroxy-7 α -(8-hydroxyoctyl)-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -(9-hydroxynonyl)-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(4,4,5,5,5-
pentafluoropentylsulfinyl)heptyl]-5 α -androstan-3-one;

- 17 β -hydroxy-7 α -[13-(4,4,5,5,5-
pentafluoropentylsulfinyl)tridecyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[7-(4,4,5,5,5-
pentafluoropentylsulfonyl)heptyl]-5 α -androstan-3-one;
5 17 β -hydroxy-7 α -[9-(4,4,5,5,5-
pentafluoropentylsulfonyl)nonyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[13-(4,4,5,5,5-
pentafluoropentylsulfonyl)tridecyl]-5 α -androstan-3-one;
17 β -hydroxy-7 α -[4-(carboxymethoxy)phenyl]-5 α -androstan-3-
10 one;
17 β -hydroxy-7 α -[4-(3-carboxypropoxy)phenyl]-5 α -androstan-3-
one;
17 β -hydroxy-11 β -[4-(3-carboxypropoxy)phenyl]-5 α -androstan-
3-one;
15 17 β -hydroxy-7 α -[4-(7-carboxyheptyloxy)phenyl]-5 α -androstan-
3-one;
17 β -hydroxy-11 β -[4-(7-carboxyheptyloxy)phenyl]-5 α -
androstan-3-one;
17 β -hydroxy-7 α -[4-(carbamoylmethoxy)phenyl]-5 α -androstan-3-
20 one;
17 β -hydroxy-7 α -[4-(carbamoylmethoxy)phenyl]-5 α -androstan-3-
one;
17 β -hydroxy-7 α -[4-(3-carbamoylpropoxy)phenyl]-5 α -androstan-
3-one;
25 17 β -hydroxy-11 β -[4-(3-carbamoylpropoxy)phenyl]-5 α -
androstan-3-one;
17 β -hydroxy-7 α -[4-(7-carbamoylheptyloxy)phenyl]-5 α -
androstan-3-one;

17 β -hydroxy-11 β -[4-{7-(4,4,5,5,5-

17 β -hydroxy-7 α -[3-{3-(3-carboxypropoxy)phenyl}propyl]-5 α -
androstan-3-one;

17 β -hydroxy-7 α -[3-[3-{3-(N-methylaminocarbonyl)propoxy}phenyl]propyl]-5 α -androstan-3-one:

17 β -hydroxy-7 α -[3-[3-{3-(1-pyrrolidinylcarbonyl)propoxy}phenyl]propyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[3-[3-{4-(N,N-dimethylaminocarbonyl)butoxy}phenyl]propyl]-5 α -androstan-3-one;

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- 5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(N,N-diethylaminocarbonyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(piperidinocarbonyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-{N-(2-furylmethyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-{7-(N-methylaminocarbonyl)heptyl}-5 α -androstan-3-one;
- 10 17 β -hydroxy-7 α -[7-(N-methyl-N-ethylaminocarbonyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(N-methyl-N-propylaminocarbonyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(N-methyl-N-
- 15 isopropylaminocarbonyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(N-methyl-N-benzylaminocarbonyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[7-(1-pyrrolidinylcarbonyl)heptyl]-5 α -androstan-3-one;
- 20 17 β -hydroxy-7 α -[7-(morpholinocarbonyl)heptyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(N,N-dimethylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(N,N-diethylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 25 17 β -hydroxy-7 α -[9-(N-methyl-N-butylaminocarbonyl)nonyl]-5 α -androstan-3-one;
- 17 β -hydroxy-7 α -[9-(N-methyl-N-propylaminocarbonyl)nonyl]-

17 β -hydroxy-7 α -[9-(morpholinocarbonyl)nonyl]-5 α -androstan-3-one:

17 β -hydroxy-7 α -[10-(N,N-dimethylaminocarbonyl)decyl]-5 α -androstane-3-one;

17 β -hydroxy-7 α -[7-{N-(2-hydroxyethyl)aminocarbonyl}heptyl]-
5 α -androstan-3-one;

17 β -hydroxy-7 α -[7-(N-propylaminocarbonyl)heptyl]-5 α -
androstan-3-one;

10 17 β -hydroxy-7 α -[7-(N-benzylaminocarbonyl)heptyl]-5 α -
androstan-3-one;

17 β -hydroxy-7 α -[7-{N-(2-phenylethyl)aminocarbonyl}heptyl]-
5 α -androstan-3-one:

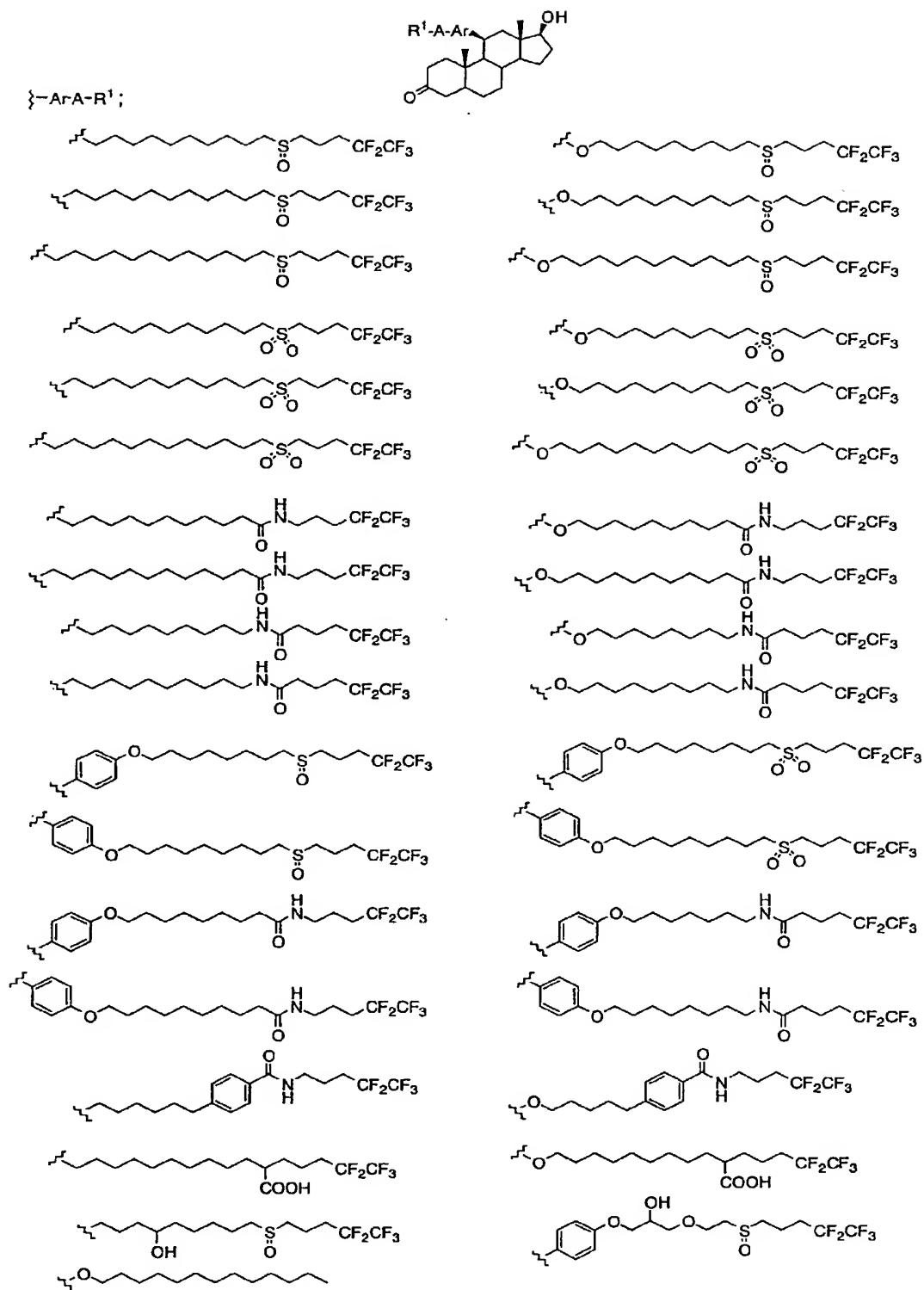
17 β -hydroxy-11 β -[9-(N,N-diethylaminocarbonyl)nonyl]-5 α -
15 androstan-3-one;

17 β -hydroxy-7 α -[3-[3-{3-(N-methylaminocarbonyl)propoxy}phenyl]propyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[3-[3-{3-(N,N-
20 dimethylaminocarbonyl)propoxy}phenyl]propyl]-5 α -androstan-
3-one:

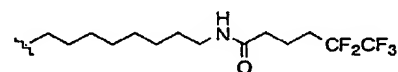
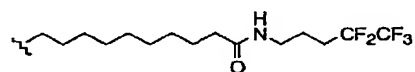
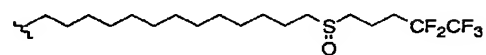
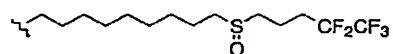
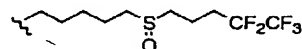
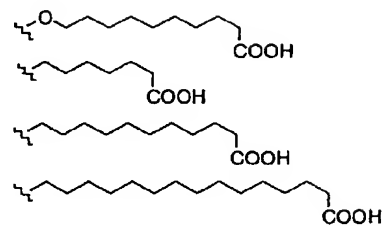
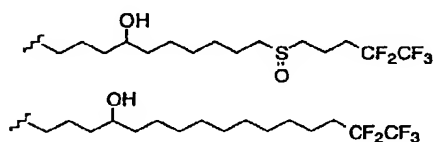
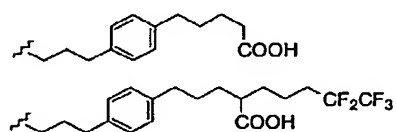
17 β -hydroxy-7 α -[3-[3-{4-(1-pyrrolidinylcarbonyl)butoxy}phenyl]propyl]-5 α -androstan-3-one.

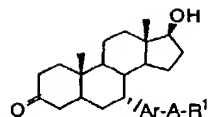
25 The structures of these compounds are shown below:

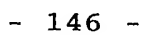
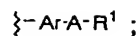


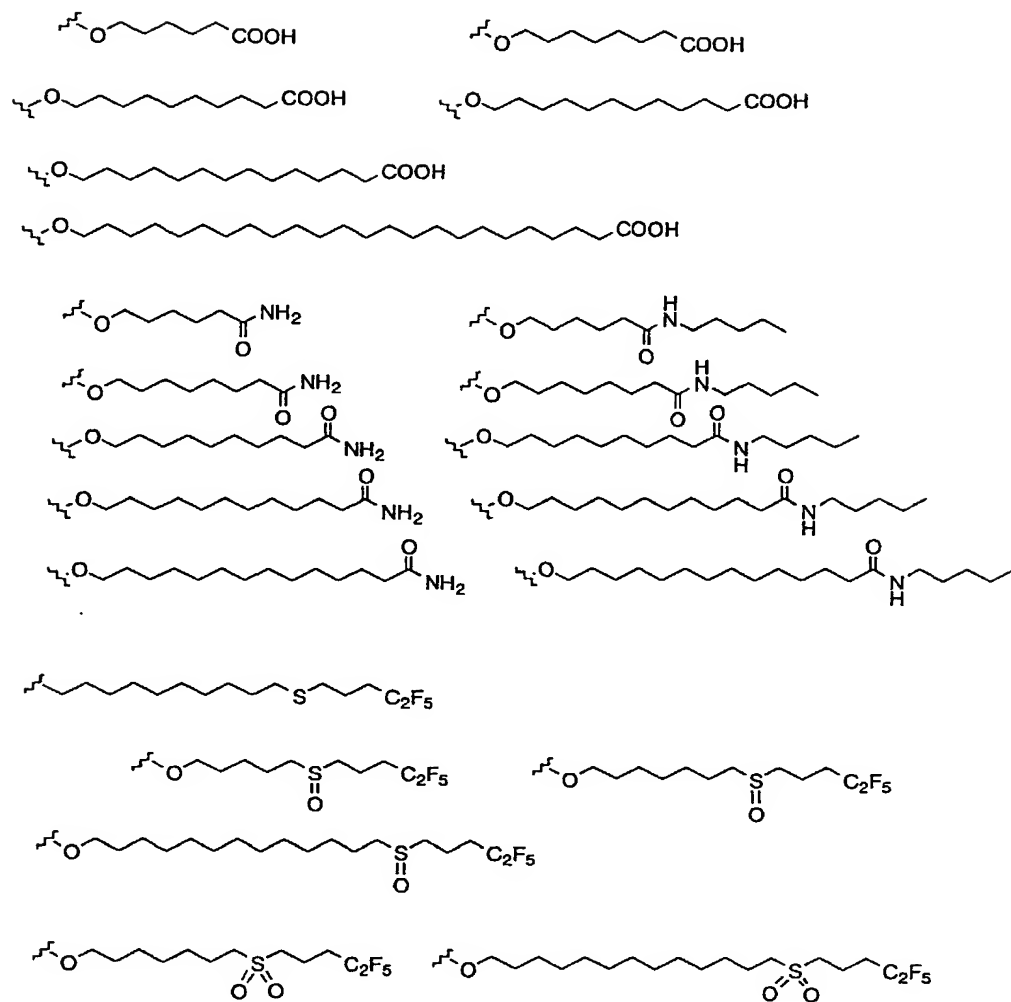
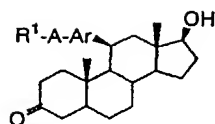
Chemical structures of the four poly(ether amine)s (PEAs) used in the study:

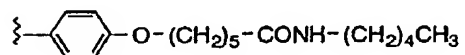
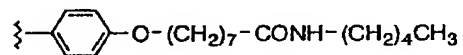
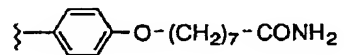
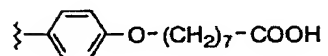
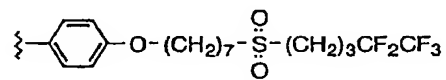
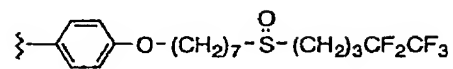
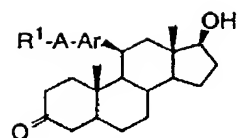
- Structure 1: Poly(ether amine) with a long polyether chain and one carboxylic acid group (COOH).
- Structure 2: Poly(ether amine) with a shorter polyether chain and one carboxylic acid group (COOH).
- Structure 3: Poly(ether amine) with a shorter polyether chain and two carboxylic acid groups (COOH).
- Structure 4: Poly(ether amine) with a long polyether chain and one carboxylic acid group (COOH).

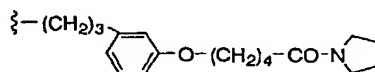
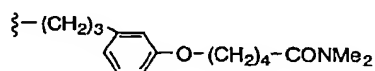
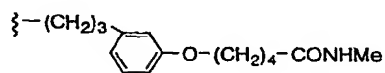
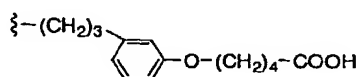
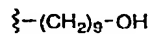
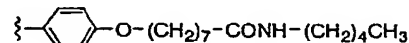
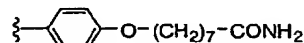
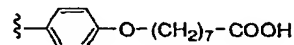
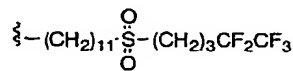
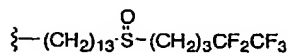
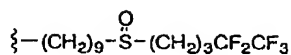
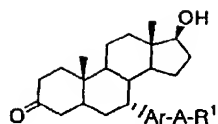












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as absolute configuration for each of the contained asymmetric carbon atoms, as well as all mixtures of those compounds at any proportions are included within the scope of the invention.

5 Speaking of the substance of the invention which acts
as antagonist against but not as agonist for the androgen
receptor, the expression "not acting as agonist" means that
in the following androgen receptor gene assay, the
transcriptional activity value of the substance at any
10 concentration of 0.1 nmol/L - 10 μ mol/L is from one to five
times the transcriptional activity value for no addition
of the substance which is taken as unity:

Twenty-four hours before transfection, 1.0×10^5 HeLa cells (purchased from Dainippon Pharmaceutical Co., Ltd.) are cultured in phenol red free Dulbecco's modified Eagle medium (DMEM) containing 5% of charcoal-treated FBS (DCC-FBS) in 12-well microplates. Five hundred nanograms/well of MMTV-Luc vector (the reporter plasmid of luciferase having mouse tumor long terminal repeats containing the androgen response element: GM-CAT vector (A.T.C.C. No. 67282) purchased from A.T.C.C. provided that the chloramphenicol acetyl transferase gene was replaced by the firefly luciferase gene), 100 ng/well of pSG5-hAR (the expression vector of the human androgen receptor which harbors the androgen receptor gene under the control of SV40 promoter) and 5 ng/well of Renilla Luc vector (a vector for internal standard incorporating the sea pansy luciferase gene) are transfected into the HeLa cells. The

transfection is performed in a liquid culture of the phenol red free DMEM using 3 mL/well of lipofectoamine (GibcoBRL). Nine hours after the transfection, the liquid culture is replaced by phenol red free DMEM/3% DCC-FBS containing 10 μ mol/L of a compound of the invention which is represented by the general formula (I) or the substance of the invention which acts as antagonist against but not as agonist for the androgen receptor. The transcriptional activity value is measured 48 hours after the replacement of the liquid culture. Transcriptional activity is measured with a dual-luciferase reporter assay system (Promega). The transcriptional activity value is defined as the value for firefly luciferase divided by the value for sea pansy luciferase. To implement this assay, reference may be had to J. Biol. Chem., vol. 270, pp. 19998-20003, 1995.

WO97/49709 mentions hydroxyflutamide (the essence of the in vivo activity of flutamide) and bicaltamide as substances that act as antagonist against but not as agonist for the androgen receptor; however, according to the definition given in that publication, the expression "not acting as agonist" means that in an androgen reporter gene assay using CV-1 cells, the agonist efficiency value represented by the following formula is 0 - 20% at a concentration of 10 μ mol/L or above and this definition is clearly and strictly distinguished from the definition of the expression "not acting as agonist" which is given in the present invention:

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Agonist efficiency (%) = (transcriptional activity value of screened non-steroid compound)/(maximum transcriptional activity value by DHT) x 100

In the androgen receptor reporter gene assay used in
5 defining the expression "not acting as agonist" in the invention, each of hydroxyflutamide and bicaltamide was found to act as agonist at a concentration of 10 μ mol/L (see Example 1 in this specification).

The expression "acting as antagonist" means that in
10 the following androgen receptor gene assay, the transcriptional activity value of 0.1 nmol/L of dihydrotestosterone (DHT) is inhibited to 0 - 50% at any concentration of 0.1 nmol/L - 10 μ mol/L:

Twenty-four hours before transfection, 1.0×10^5 HeLa
15 cells are cultured in phenol red free DMEM/5% DCC-FBS on 12-well microplates. Five hundred nanograms/well of MMTV-Luc vector, 100 ng/well of pSG5/hAR and 5 ng/well of Renilla Luc vector are transfected into the HeLa cells. The transfection is performed in a liquid culture of the
20 phenol red free DMEM using 3 mL/well of lipofectoamine. Nine hours after the transfection, the liquid culture is replaced by phenol red free DMEM/3% DCC-FBS containing 0.1 nmol/L of DHT and 1.0 mol/L of a compound of the invention which is represented by the general formula (I) or the
25 substance of the invention which acts as antagonist against but not as agonist for the androgen receptor. The transcriptional activity value is measured 48 hours after the replacement of the liquid culture. Transcriptional

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activity is measured with a dual-luciferase reporter assay system. The transcriptional activity value is defined as the value for firefly luciferase divided by the value for sea pansy luciferase. To implement this assay, reference
5 may be had to J. Biol. Chem., vol. 270, pp. 19998-20003, 1995.

Specific examples of the substance of the invention which acts as antagonist against but not as agonist for the androgen receptor may include compounds of the invention
10 which are represented by the general formula (I).

The compounds of the invention which are represented by the general formula (I) and the substance of the invention which acts as antagonist against but not as agonist for the androgen receptor can also be obtained as
15 their pharmaceutically acceptable salts. Pharmaceutically acceptable salts include inorganic acid salts such as hydrochlorides, hyrobromides, hydroiodides, sulfates and phosphates; organic acid salts such as formates, acetates, oxalates, maleates, fumarates, methanesulfonates,
20 benzenesulfonates, p-toluenesulfonates, succinates, malonates, citrates, gluconates, mandelates, benzoates, salicylates, trifluoroacetates, tartrates, propionates and glutarates; inorganic base salts such as sodium salts, potassium salts, magnesium salts and zinc salts; and
25 organic base salts such as ammonium salts.

The compounds of the invention which are represented by the general formula (I), their pharmaceutically acceptable salts, as well as the substance of the invention

which acts as antagonist against but not as agonist for the androgen receptor, and its pharmaceutically acceptable salts can also be obtained as their prodrugs. The prodrugs mean those compounds which undergo rapid transformation in living body to generate, typically by hydrolysis in the blood, the compounds of the invention which are represented by the general formula (I), their pharmaceutically acceptable salts, as well as the substance of the invention which acts as antagonist against but not as agonist for the androgen receptor, and its pharmaceutically acceptable salts. T. Higuchi and V. Stella give detailed accounts of the concept of prodrugs in "Prodrugs as Novel Delivery Systems", vol. 14 of the A.C.S. Symposium Series, American Chemical Society (1975). These prodrugs may or may not have activity on their own but they usually have little activity. Reference may also be had to D.E.V. Wilman, "Prodrugs in Cancer Chemotherapy" in Biochemical Society Transactions, vol. 14, pp. 375-382, the 615th Meeting, Belfast, 1986, and V.J. Stella et al., "Prodrugs: Chemical Methods for Targeted Drug Delivery" in Directed Drug Delivery, ed. by R. Borchardt et al., pp. 247-267, Humana Press, 1985. If compounds of the invention which are represented by the general formula (I) have the -COOH partial structure, specific examples of prodrugs include esters, carbonates, carbamates, etc. of such compounds.

The compounds of the invention which are represented by the general formula (I) can typically be produced by process A to process W, process B' to process L', process

carbon atoms, preferably ethane-1,2-diyl group, propane-1,3-diyl group and butane-1,4-diyl group.

R^4 represents the general formula (V)



5 (wherein G^3 represents a straight-chained or branched alkylene group having 1 - 27 carbon atoms, a straight-chained or branched alkenylene group having 2 - 27 carbon atoms or a straight-chained or branched alkynylene group having 2 - 27 carbon atoms; E, J, Y, L, Q^2 and Z have the
10 same meanings as defined above); R^5 represents a halogen atom, preferably a bromine atom or an iodine atom; R^6 represents a substituted silyl group, preferably trimethylsilyl group; R^{13} represents a straight-chained or branched alkyl group having 1 - 6 carbon atoms that may
15 optionally be substituted by a halogen atom, preferably trifluoromethyl group or 1,1,2,2,3,3,4,4,4-nonafluorobutyl group; R^{14} represents a group represented by $-MgR^5$, $-ZnR^5$ or $-Sn(R^7)_3$, preferably a group represented by $-Sn(R^7)_3$; G^4 represents a straight-chained or branched alkylene group
20 having 1 - 30 carbon atoms, a straight-chained or branched alkenylene group having 2 - 30 carbon atoms or a straight-chained or branched alkynylene group having 2 - 30 carbon atoms; the wavy line represents a single bond of trans configuration or cis configuration, preferably trans
25 configuration, with respect to the double bond.

Process A is for producing compound (6) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula

(II) in which Ar is a single bond, A is -O- and R¹ is -CH₂-CH=CH-CH₂-R², X² is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the

5 dashed line together with the solid line is a single bond or a double bond; compound (7) represented by the general formula (I) in which X¹ is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R¹ is -(CH₂)₄-R², X² is a hydrogen

10 atom, R^a is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond; compound (9) represented by the general formula (I) in which X¹ is a

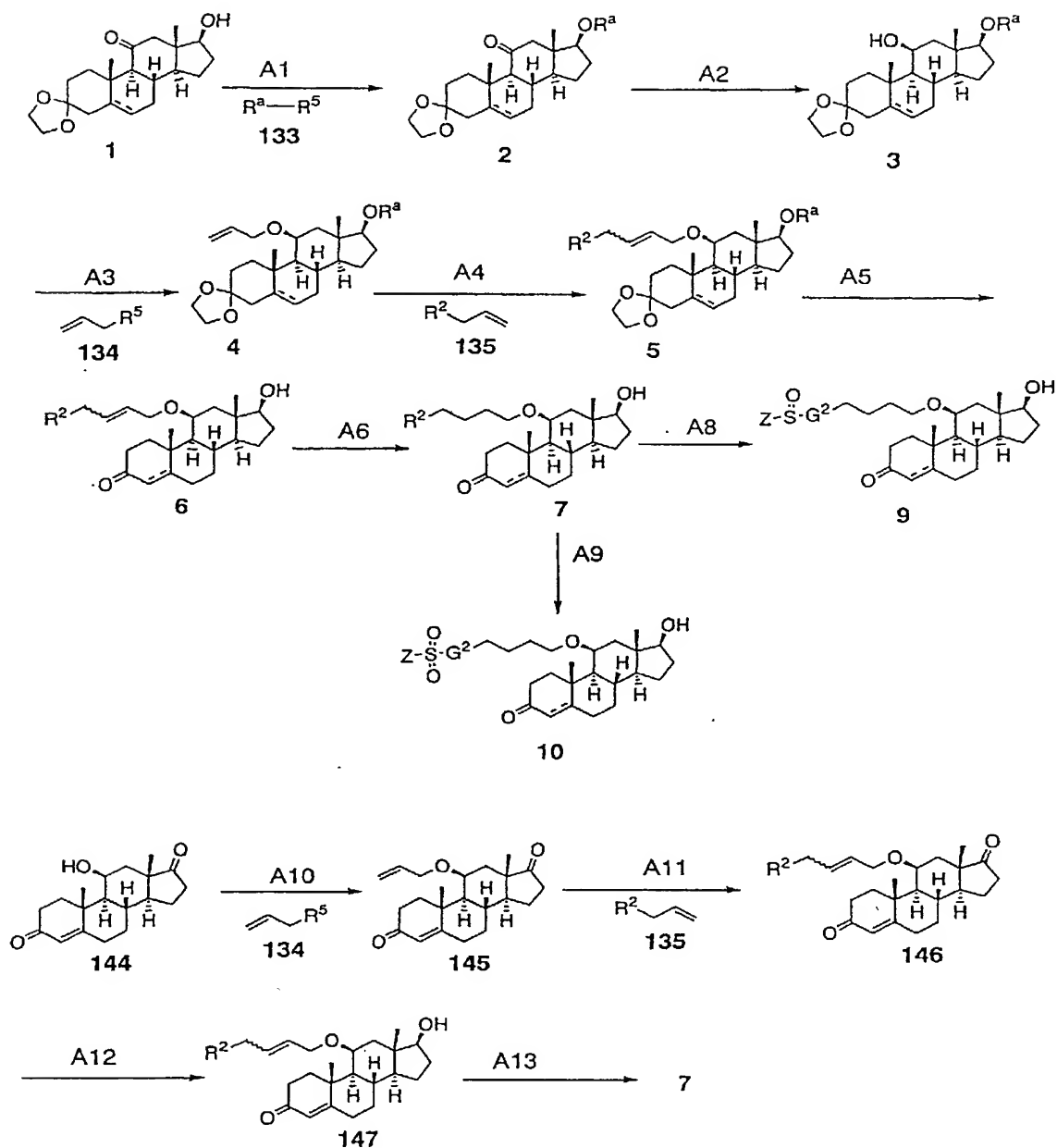
15 group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R¹ is -(CH₂)₄-G²-S(O)-Z, X² is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the

20 dashed line together with the solid line is a single bond or a double bond; compound (10) represented by the general formula (I) in which X¹ is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R¹ is -(CH₂)₄-G²-S(O)₂-Z, X² is a

25 hydrogen atom, R^a is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond; and

compound (147) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R^1 is $-\text{CH}_2-\text{CH}=\text{CH}-\text{CH}_2-\text{R}^2$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a double bond.

Process A



Step A1 is for producing compound (2) and implemented by reacting compound (1) with compound (133) in an inert solvent in the presence of a base.

5 The inert solvent to be used is not limited in any particular way as long as it does not participate in the

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trimethoxyaluminum lithium hydride, tri-t-butoxyaluminum lithium hydride, aluminum lithium hydride-trichloroaluminum (alane), aluminum lithium hydride-boron trifluoride, aluminum hydride magnesium chloride, magnesium aluminum hydride, sodium aluminum hydride, sodium triethoxyaluminum hydride, sodium bis(methoxyethoxy)aluminum hydride, sodium boron hydride, sodium boron hydride-palladium/carbon, sodium boron hydrogensulfide, sodium boron hydrogencyanide, sodium trimethoxyboron hydride, lithium boron hydride, lithium boron hydrogencyanide, lithium triethylboron hydride, lithium tri-s-butylboron hydride, lithium tri-t-butylboron hydride, calcium boron hydride, potassium boron hydride, potassium triisopropoxyboron hydride, potassium tri-s-butylboron hydride, zinc boron hydride, tetramethylammonium boron hydride, and tetra-n-butylammonium cyanoboron hydride; metal hydrides such as diisobutylaluminum hydride, triphenyltin hydride, tri-n-butyltin hydride, diphenyltin hydride, di-n-butyltin hydride, triethyltin hydride, trimethyltin hydride, trichlorosilane/tri-n-butylamine, trichlorosilane/tri-n-propylamine, triethylsilane, trimethylsilane, diphenylsilane, phenylsilane, polymethylhydrosiloxane, dimethylphenylsilane, di-n-butylsilane, and methylphenylsilane; borane derivatives such as diborane, dimethylamine-borane, trimethylamine-borane, ethylenediamine-borane, pyridine-borane, dimethylsulfide-borane, 2,3-dimethyl-2-butylborane (thexylborane), bis-3-methyl-2-butylborane (disiamylborane),

diisopinocanepherylborane, dicyclohexylborane, and 9-borabicyclo[3,3,1]nonane (9-BBN); preferred examples are metal hydrogen complex compounds such as aluminum lithium hydride, trimethoxyaluminum lithium hydride, tri-t-butoxyaluminum lithium hydride, aluminum lithium hydride-trichloroaluminum (alane), aluminum lithium hydride-boron trifluoride, aluminum hydride magnesium chloride, magnesium aluminum hydride, sodium aluminum hydride, sodium triethoxyaluminum hydride, sodium

10 bis(methoxyethoxy)aluminum hydride, sodium boron hydride, sodium boron hydride-palladium/carbon, sodium boron hydrogensulfide, sodium boron hydrogencyanide, sodium trimethoxyboron hydride, lithium boron hydride, lithium boron hydrogencyanide, lithium triethylboron hydride,

15 lithium tri-s-butylboron hydride, lithium tri-t-butylboron hydride, calcium boron hydride, potassium boron hydride, potassium triisopropoxyboron hydride, potassium tri-s-butylboron hydride, zinc boron hydride, tetramethylammonium boron hydride, and tetra-n-butylammonium cyanoboron hydride,

20 with aluminum lithium hydride being more preferred. The reaction temperature which varies with the type of solvent and the like is typically in the range of -30°C ~ 100°C, preferably 0°C ~ 70°C. The reaction time which varies with the reaction temperature and the like is typically in the

25 range of 10 minutes - 48 hours, preferably 30 minutes - 24 hours.

As a by-product of this step, there is formed a compound having the hydroxyl group in 11-position of

compound (3) oriented in α configuration and this compound may be used to prepare compounds having X^1 in compound (6), compound (7), compound (9) and compound (10) oriented in α configuration.

5 Step A3 is for producing compound (4) and implemented by reacting compound (3) with a base in an inert solvent to make a salt of compound (3) and then reacting it with compound (134) in an inert solvent.

 The inert solvent to be used is not limited in any
10 particular way as long as it does not participate in the reaction; examples are halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, aromatic solvents such as benzene, toluene,
15 xylene, quinoline and chlorobenzene, as well as cyclohexane, dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone, dimethylformamide, and N-methylpyrrolidone; preferred examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane,
20 as well as dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone, dimethylformamide, and N-methylpyrrolidone. The base to be used may be exemplified by metal hydrides such as sodium hydride, potassium hydride and calcium hydride, alkyl lithium compounds such as
25 methyl lithium, ethyl lithium, n-butyl lithium and t-butyl lithium, metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide, potassium hydroxide, calcium hydroxide, barium hydroxide and cesium hydroxide,

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metal amides such as sodium amide, potassium bistrimethylsilylamide, sodium bistrimethylsilylamide and lithium diisopropylamide, amines such as triethylamine, diisopropylethylamine, 1,8-diazabicyclo[5.4.0]-7-undecene, pyridine, dimethylamionopyridine and pyrazine, as well as sodium tetraborate, sodium iodide, lithium hexamethyldisilazane, sodium hexamethyldisilazane and potassium hexamethyldisilazane; preferred examples are metal hydrides such as sodium hydride, potassium hydride and calcium hydride, and alkyl lithium compounds such as methyl lithium, ethyl lithium, n-butyl lithium and t-butyl lithium. The reaction temperature which varies with the type of solvent and the like is typically in the range of -30°C ~ 100°C, preferably 0°C ~ 70°C. The reaction temperature which varies with the reaction temperature and the like is typically in the range of 10 minutes - 48 hours, preferably 30 minutes - 24 hours.

Step A4 is for producing compound (5) and implemented by reacting compound (4) with compound (135) in an inert solvent in the presence of an organometallic catalyst.

The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction; preferred examples are halogen-containing solvents such as dichloromethane and chloroform, ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, and aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, with dichloromethane and dimethoxyethane being more preferred.

by performing catalytic reduction in an alcoholic solvent or an inert solvent.

The solvent to be used may be exemplified by alcoholic solvents such as methanol, ethanol, n-propanol, i-propanol, 5 n-butanol, s-butanol, t-butanol, pentanol, hexanol, cyclopropanol, cyclobutanol, cyclopentanol, cyclohexanol, ethylene glycol, 1,3-propanediol, 1,4-butanediol and 1,5-pentanediol, ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, aromatic solvents such as 10 benzene, toluene, xylene, quinoline and chlorobenzene, halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, as well as cyclohexane, dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone, dimethylformamide, N- 15 methylpyrrolidone, ethyl acetate, acetonitrile and nitromethane; preferred examples are ethanol, dioxane, benzene and ethyl acetate.

The condition to be used in catalytic reduction is a homogeneous system such as hydrogen- 20 chlorotris(triphenylphosphine)rhodium(I), hydrogen-chlorotris(triparatolyphosphine)rhodium(I), hydrogen-chlorotris(triparamethoxyphenylphosphine)rhodium(I), hydrogen-hydridecarbonyltris(triphenylphosphine)rhodium(I), hydrogen-rhodium(II) acetate, hydrogen-ruthenium(II) 25 acetate, hydrogen-chlorohydridetris(triphenylphosphine) ruthenium(II), hydrogen-carboxylatohydridetris(triphenylphosphine)ruthenium(II), hydrogen-hydridecarbonyltris(triphenylphosphine)iridium(I),

- hydrogen-platinum(II)-tin chloride complex, hydrogen-pentacyanocobalt(II) complex, hydrogen-tricyanobipyridine cobalt(II) complex, hydrogen-bis(dimethylglyoximato)cobalt(II) complex, hydrogen-methyl
- 5 benzoate-tricarbonylchromium complex, hydrogen-bis(tricarbonylcyclopentadienylchromium), hydrogen-pentacarbonyliron, hydrogen-bis(cyclopentadienyl)dicarbonyltitanium, hydrogen-hydridecarbonylcobalt complex, hydrogen-
- 10 octacarbonyldicobalt, hydrogen-hydridecarbonylrhodium, hydrogen-chromium(III) acetylacetonato-triisobutylaluminum, hydrogen-cobalt(II) acetylacetonato-triisobutylaluminum, or hydrogen-nickel(II)-2-hexanoato-triethylaluminum, or an inhomogeneous system condition such as hydrogen-platinum
- 15 dioxide, hydrogen-platinum/carbon, hydrogen-palladium/carbon, hydrogen-palladium/barium sulfate, hydrogen-palladium/calcium carbonate, hydrogen-Raney nickel, hydrogen-copper chromite, hydrogen-rhodium/carbon, hydrogen-rhodium/alumina, hydrogen-ruthenium dioxide, or
- 20 hydrogen-ruthenium/carbon; preferred examples are hydrogen-chlorotris(triphenylphosphine)rhodium(I), hydrogen-palladium/carbon, hydrogen-palladium/calcium carbonate, etc.

The reaction temperature is typically in the range of 0°C - 100°C, preferably 0°C - 60°C. The reaction time which

25 varies with the reaction temperature and the like is typically in the range of 10 minutes - 24 hours, preferably 10 minutes - 6 hours.

Step A8 is for producing compound (9) in the case

where Q^2 in R^2 in compound (7) is -S- and implemented by reacting compound (7) with an oxidizing agent in an inert solvent.

The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction and examples include halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, alcoholic solvents such as methanol and ethanol, ether solvents such as tetrahydrofuran, as well as water, and mixtures thereof; preferred examples are dichloromethane, methanol and a mixture of tetrahydrofuran and water.

The oxidizing agent to be used may be exemplified by organic peroxides such as t-butyl perbenzoate, t-butyl peracetate, t-butyl hydroperoxide, t-amyl hydroperoxide, dibenzoyl peroxide, di-p-nitrobenzoyl peroxide and di-p-chlorobenzoyl peroxide, organic peracids such as perbenzoic acid, metachloroperbenzoic acid, p-nitroperbenzoic acid, monoperoxyphthalic acid, performic acid, peracetic acid, trifluoroperacetic acid and peroxyauric acid, halogens such as hypochlorous acid, sodium hypochlorite, potassium hypobromite, potassium hypoiodite, sodium chlorate, potassium chlorate, sodium bromate, potassium bromate, sodium iodate, potassium iodate, perchloryl fluoride, orthoperiodic acid, sodium metaperiodate, potassium metaperiodate, N-bromoacetamide, N-bromosuccinimide, N-bromophthalimide, isocyanuric chloride, isocyanuric bromide,

N-bromocaprolactam, 1-chlorobenzotriazole, 1,3-dibromo-5,5-dimethylhydantoin, sodium N-chloro-p-toluenesulfonamide (chloramine T), sodium N-chlorobenzenesulfonamide (chloramine B), t-butyl hypochlorite, t-butyl hypobromite, 5 t-butyl hypoiodite, iodosylbenzene acetate and iodosylbenzene, as well as peroxomonosulfuric acid, OXONE (registered trademark) and hydrogen peroxide; preferred examples are sodium periodate and OXONE (registered trademark).

10 The reaction temperature which varies with the type of solvent and the like is typically in the range of -20°C ~ 30°C (preferably -10°C ~ 10°C). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably 15 30 minutes - 15 hours).

Step A9 is for producing compound (10) in the case where Q^2 in R^2 in compound (7) is -S- and implemented by reacting compound (7) with an oxidizing agent in an inert solvent.

20 The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction and examples include halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, aromatic solvents such as benzene, toluene, 25 xylene, quinoline and chlorobenzene, alcoholic solvents such as methanol and ethanol, ether solvents such as tetrahydrofuran, as well as water, and mixtures thereof; preferred examples are dichloromethane, methanol and a

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mixture of tetrahydrofuran and water.

The oxidizing agent to be used may be exemplified by organic peroxides such as t-butyl perbenzoate, t-butyl peracetate, t-butyl hydroperoxide, t-amyl hydroperoxide, 5 dibenzoyl peroxide, di-p-nitrobenzoyl peroxide and di-p-chlorobenzoyl peroxide, organic peracids such as perbenzoic acid, metachloroperbenzoic acid, p-nitroperbenzoic acid, monoperoxyphthalic acid, performic acid, peracetic acid, trifluoroperacetic acid and peroxyauric acid, halogens 10 such as hypochlorous acid, sodium hypochlorite, potassium hypobromite, potassium hypoiodite, sodium chlorate, potassium chlorate, sodium bromate, potassium bromate, sodium iodate, potassium iodate, perchloryl fluoride, orthoperiodic acid, sodium metaperiodate, potassium 15 metaperiodate, N-bromoacetamide, N-bromosuccinimide, N-bromophthalimide, isocyanuric chloride, isocyanuric bromide, N-bromocaprolactam, 1-chlorobenzotriazole, 1,3-dibromo-5,5-dimethylhydantoin, sodium N-chloro-p-toluenesulfonamide (chloramine T), sodium N-chlorobenzenesulfonamide 20 (chloramine B), t-butyl hypochlorite, t-butyl hypobromite, t-butyl hypoiodite, iodosylbenzene acetate and iodosylbenzene, as well as peroxomonosulfuric acid, OXONE (registered trademark) and hydrogen peroxide; a preferred example is OXONE (registered trademark).

25 The reaction temperature which varies with the type of solvent and the like is typically in the range of 0 °C ~ 100 °C (preferably 10°C ~ 50°C). The reaction time which varies with the reaction temperature and the like is

typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 15 hours).

Step A10 is for producing compound (145) and implemented by reacting compound (144) with a base in an inert solvent to make a salt of compound (144) and then reacting it with compound (134) in an inert solvent. The reaction is performed as in the aforementioned step A3 in process A.

A compound having the hydroxyl group in 11-position of compound (144) oriented in β configuration is commercially available and using this compound in place of compound (144), one can obtain a compound having X^1 in compound (7) oriented in β configuration.

Step A11 is for producing compound (146) and implemented by reacting compound (145) with compound (135) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the aforementioned step A4 in process A.

Step A12 is for producing compound (147) and implemented by reacting compound (146) with a reducing agent in an optionally miscible inert solvent.

The inert solvent to be used is not limited in any particular way as long as it does not interfere with the reaction; examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, alcoholic solvents such as methanol and ethanol, aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, and amines such as pyridine and

such as diborane, dimethylamine-borane, trimethylamine-borane, ethylenediamine-borane, pyridine-borane, dimethylsulfide-borane, 2,3-dimethyl-2-butylborane (thexylborane), bis-3-methyl-2-butylborane (disiamylborane),
5 diisopinocampheylborane, dicyclohexylborane, and 9-borabicyclo[3,3,1]nonane (9-BBN); preferred examples are metal hydrogen complex compounds such as aluminum lithium hydride, trimethoxyaluminum lithium hydride, tri-t-butoxyaluminum lithium hydride, aluminum lithium hydride-
10 trichloroaluminum (alane), aluminum lithium hydride-boron trifluoride, aluminum hydride magnesium chloride, magnesium aluminum hydride, sodium aluminum hydride, sodium triethoxyaluminum hydride, sodium bis(methoxyethoxy)aluminum hydride, sodium boron hydride,
15 sodium boron hydride-palladium/carbon, sodium boron hydrosulfide, sodium boron hydrogencyanide, sodium trimethoxyboron hydride, lithium boron hydride, lithium boron hydrogencyanide, lithium triethylboron hydride, lithium tri-s-butylboron hydride, lithium tri-t-butylboron
20 hydride, calcium boron hydride, potassium boron hydride, potassium triisopropoxyboron hydride, potassium tri-s-butylboron hydride, zinc boron hydride, tetramethylammonium boron hydride, and tetra-n-butylammonium cyanoboron hydride, with sodium boron hydride being more preferred. The
25 reaction temperature which varies with the type of solvent and the like is typically in the range of -30°C ~ 100°C, preferably 0°C ~ 70°C. The reaction time which varies with the reaction temperature and the like is typically in the

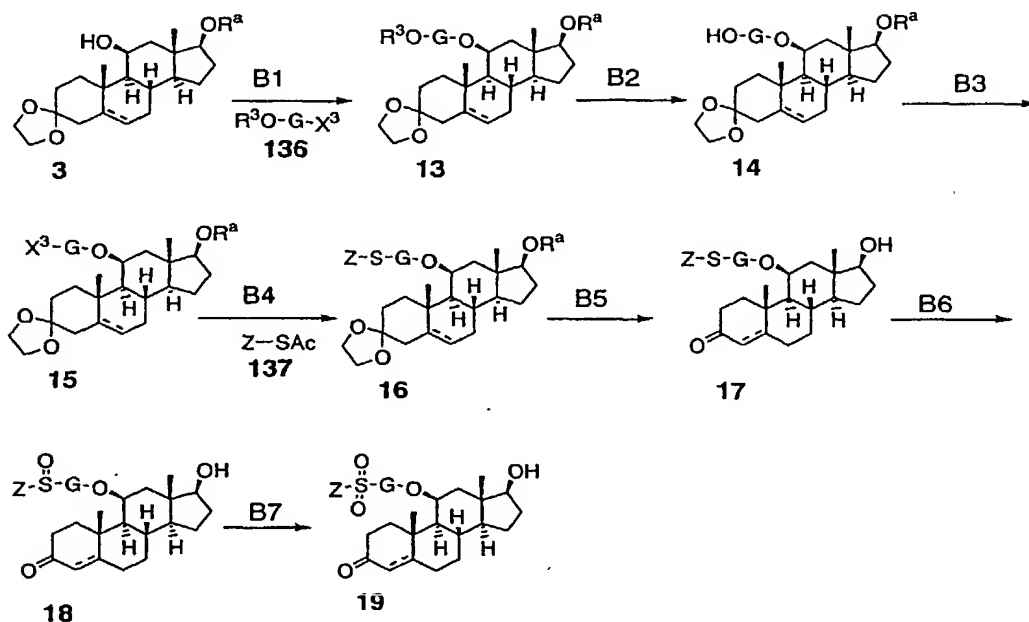
range of 10 minutes - 48 hours, preferably 30 minutes - 24 hours.

Step A13 is for producing compound (7) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the
5 aforementioned step A6 in process A.

Process B is for producing compound (17) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula
10 (II) in which Ar is a single bond, A is -O- and R^1 is -G-S-Z, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double
15 bond; compound (18) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R^1 is -G-S(O)-Z-, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together
20 with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond; and compound (19) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general
25 formula (II) in which Ar is a single bond, A is -O- and R^1 is -G-S(O)₂-Z, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the

dashed line together with the solid line is a single bond or a double bond.

Process B



5 Step B1 is for producing compound (13) and implemented by reacting compound (3) with a base in an inert solvent to make a salt of compound (3) and then reacting it with compound (136) in an inert solvent. The reaction is performed as in the aforementioned step A3 in process A.

10 Step B2 is for producing compound (14) and implemented by reacting compound (13) with a deprotecting agent, namely by removing the substituted silyl group, in an inert solvent.

15 The inert solvent to be used is not limited in a particular way as long as it does not interfere with the reaction; examples include ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, as well as

dimethylformamide and water, with tetrahydrofuran being preferred. The deprotecting agent to be used is not limited in any particular way and may be exemplified by fluorides such as hydrogen fluoride, hydrogen fluoride-
5 pyridine, sodium fluoride, potassium fluoride and tetra-n-butylammonium fluoride, and organic acids such as formic acid, acetic acid and p-toluenesulfonic acid, with tetra-n-butylammonium fluoride being preferred.

The reaction temperature which varies with the type of
10 solvent and the like is typically in the range of 0°C - 80°C (preferably 0°C - 50°C). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 15 hours).

15 Step B3 is for producing compound (15) and implemented by reacting compound (14) with a sulfonyl chloride compound in an amine-containing solvent or reacting compound (14) with a halogenating agent in an inert solvent.

The amine-containing solvent to be used is not limited
20 in any particular way and may be exemplified by triethylamine, diisopropylethylamine, 1,8-diazabicyclo[5.4.0]-7-undecene and pyridine, with pyridine and triethylamine being preferred.

The sulfonyl chloride compound to be used is not
25 limited in any particular way and may be exemplified by p-toluenesulfonyl chloride, benzenesulfonyl chloride, methanesulfonyl chloride and trifluoromethanesulfonyl chloride, with methanesulfonyl chloride and

trifluoromethanesulfonyl chloride being preferred.

The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction of interest; examples include ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, nitrile-containing solvents such as acetonitrile, halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, as well as cyclohexane, dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone, dimethylformamide, N-methylpyrrolidone and ethyl acetate, with benzene and dichloromethane being preferred.

The halogenating agent to be used may be exemplified by chlorinating agents such as carbon tetrachloride-triphenylphosphine, thionyl chloride, sulfuryl chloride, N-chlorosuccinimide-triphenylphosphine, N-chlorosuccinimide-dimethyl sulfide, phosphorus trichloride and phosphorus pentachloride, and brominating agents such as carbon tetrabromide-triphenylphosphine, N-bromosuccinimide-triphenylphosphine, N-bromosuccinimide-dimethyl sulfide, phosphorus tribromide and phosphorus pentabromide, and preferred examples are carbon tetrabromide-triphenylphosphine and thionyl chloride. The reaction temperature is typically in the range of 0°C - 80°C, preferably 10°C - 40°C. The reaction time which varies with the reaction temperature is typically in the range of 10 minutes - 10 hours, preferably 30 minutes - 3 hours.

Step B4 is for producing compound (16) and implemented by reacting compound (137) with a metal alkoxide in an alcoholic solvent to make a reactive derivative of compound (137) and then reacting it with compound (15) in an
5 alcoholic solvent.

The alcoholic solvent to be used is not limited in any particular way and may be exemplified by methanol, ethanol, n-propanol, i-propanol and mixed solvents containing them, and preferred examples are methanol and a methanol-
10 tetrahydrofuran mixed solvent.

The metal alkoxide to be used is not limited in any particular way and may be exemplified by sodium methoxide and sodium ethoxide, with sodium methoxide being preferred.

The reaction temperature which varies with the solvent
15 and other conditions is typically in the range of 0°C - 80°C, preferably 10°C - 40°C. The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 10 hours, preferably 30 minutes - 8 hours.

20 Step B5 is for producing compound (17) and implemented by reacting compound (16) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step A5 in process A.

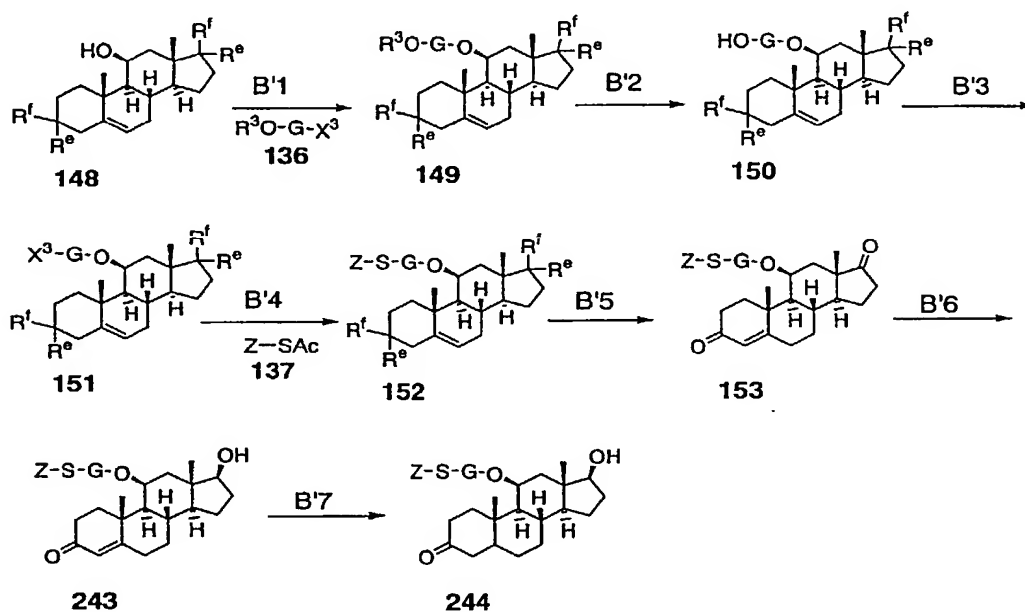
Step B6 is for producing compound (18) and implemented
25 by reacting compound (17) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A8 in process A.

Step B7 is for producing compound (19) and implemented

by reacting compound (18) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A9 in process A.

Process B' is an alternative method for producing compound (243) having the dashed line in compound (17) forming a double bond together with the solid line and compound (244) having the dashed line in compound (17) forming a single bond together with the solid line.

Process B'



10

Step B'1 is for producing compound (149) and implemented by reacting compound (148) with a base in an inert solvent to make a salt of compound (148) and then reacting it with compound (136) in an inert solvent. The reaction is performed as in the aforementioned step A3 in process A.

Step B'2 is for producing compound (150) and

implemented by reacting compound (149) with a deprotecting agent, namely by removing the substituted silyl group, in an inert solvent. The reaction is performed as in the aforementioned step B2 in process B.

5 Step B'3 is for producing compound (151) and implemented by reacting compound (150) with a sulfonyl chloride compound in an amine-containing solvent or reacting compound (150) with a halogenating agent in an inert solvent. The reaction is performed as in the
10 aforementioned step B3 in process B.

 Step B'4 is for producing compound (152) and implemented by reacting compound (137) with a metal alkoxide in an alcoholic solvent to make a reactive derivative of compound (137) and then reacting it with
15 compound (151) in an alcoholic solvent. The reaction is performed as in the aforementioned step B4 in process B.

 Step B'5 is for producing compound (153) and implemented by reacting compound (152) with an acid in an aqueous solvent. The reaction is performed as in the
20 aforementioned step A5 in process A.

 Step B'6 is for producing compound (243) and implemented by reacting compound (153) with a reducing agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step A12 in
25 process A.

 Step B'7 is for producing compound (244) and implemented by performing catalytic reduction of compound (243) in an alcoholic solvent or an inert solvent or

reducing compound (243) with a reducing agent in an optionally miscible inert solvent.

The solvent to be used in performing catalytic reduction

20 The condition to be used in catalytic reduction is a
homogeneous system such as hydrogen-
chlorotris(triphenylphosphine)rhodium(I), hydrogen-
chlorotris(triparatolyolphosphine)rhodium(I), hydrogen-
chlorotris(triparamethoxyphenylphosphine)rhodium(I),
25 hydrogen-hydridecarbonyltris(triphenylphosphine)rhodium(I),
hydrogen-rhodium(II) acetate, hydrogen-ruthenium(II)
acetate, hydrogen-
chlorohydridetris(triphenylphosphine)ruthenium(II),

hydrogen-
carboxylatohydridetris(triphenylphosphine)ruthenium(II),
hydrogen-hydridecarbonyltris(triphenylphosphine)iridium(I),
hydrogen-platinum(II)-tin chloride complex, hydrogen-
5 pentacyanocobalt(II) complex, hydrogen-tricyanobipyridine
cobalt(II) complex, hydrogen-
bis(dimethylglyoximato)cobalt(II) complex, hydrogen-methyl
benzoate-tricarbonylchromium complex, hydrogen-
bis(tricarbonylcyclopentadienylchromium), hydrogen-
10 pentacarbonyliron, hydrogen-
bis(cyclopentadienyl)dicarbonyltitanium, hydrogen-
hydridecarbonylcobalt complex, hydrogen-
octacarbonyldicobalt, hydrogen-hydridecarbonylrhodium,
hydrogen-chromium(III) acetylacetonato-triisobutylaluminum,
15 hydrogen-cobalt(II) acetylacetonato-triisobutylaluminum, or
hydrogen-nickel(II)-2-hexanoato-triethylaluminum, or an
inhomogeneous system condition such as hydrogen-platinum
dioxide, hydrogen-platinum/carbon, hydrogen-
palladium/carbon, hydrogen-palladium/barium sulfate,
20 hydrogen-palladium/calcium carbonate, hydrogen-Raney nickel,
hydrogen-copper chromite, hydrogen-rhodium/carbon,
hydrogen-rhodium/alumina, hydrogen-ruthenium dioxide, or
hydrogen-ruthenium/carbon; preferred examples are hydrogen-
chlorotris(triphenylphosphine)rhodium(I), hydrogen-
25 palladium/carbon, hydrogen-palladium/calcium carbonate, etc.

The reaction temperature is typically in the range of 0°C - 100°C, preferably 0°C - 60°C. The reaction time which varies with the reaction temperature and the like is

typically in the range of 10 minutes - 24 hours, preferably 10 minutes - 6 hours.

The inert solvent to be used in the reaction with the reducing agent is not limited in any particular way as long as it does not participate in the reaction; examples include ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, amine-containing solvents such as pyridine and triethylamine, as well as cyclohexane, dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone, dimethylformamide, N-methylpyrrolidone, acetonitrile and nitromethane; preferred examples are tetrahydrofuran, benzene, toluene and pyridine.

The reducing agent to be used may be exemplified by metals such as sodium/liquid ammonia, lithium/liquid ammonia, lithium/methylamine, lithium/ethylamine, lithium/ethylenediamine, sodium/hexamethylphosphamide-t-butanol, sodium/ethanol, sodium/t-butanol-tetrahydrofuran and sodium/toluene-t-amyl alcohol, metal hydrides such as triphenyltin hydride, tri-n-butyltin hydride, diphenyltin hydride, di-n-butyltin hydride, triethyltin hydride, trimethyltin hydride, trichlorosilane/tri-n-butylamine, trichlorosilane/tri-n-propylamine, triethylsilane, trimethylsilane, diphenylsilane, phenylsilane, polymethylhydrosiloxane, dimethylphenylsilane, di-n-butylsilane and methylphenylsilane, metal hydrogen complex

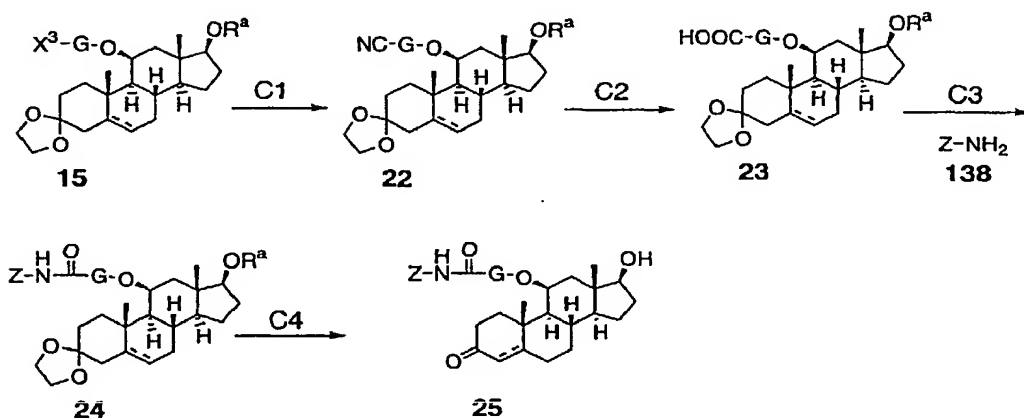
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CONH-Z, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond.

Process C



Step C1 is for producing compound (22) and implemented by reacting compound (15) with a cyanylating agent in an inert solvent.

The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction; examples include ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, as well as cyclohexane, dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone, dimethylformamide, N-methylpyrrolidone, methyl acetate, acetonitrile and

nitromethane; a preferred example is dimethyl sulfoxide.

The cyanlyating agent to be used may be exemplified by lithium cyanide, sodium cyanide, potassium cyanide, etc. and sodium cyanide is preferred. The reaction temperature is typically in the range of 0°C - 80°C, preferably 10°C - 40°C. The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 24 hours, preferably 1 hour - 15 hours.

Step C2 is for producing compound (23) and implemented by hydrolyzing compound (22) in the presence of a base.

The solvent to be used is not limited in any particular way as long as it is used in ordinary hydrolytic reaction; examples can be alcoholic solvents such as methanol and ethanol, ether solvents such as tetrahydrofuran and dioxane, water, and mixtures thereof; preferred examples are water and hydrous alcoholic solvents such as water-ethanol.

The base to be used is not limited in any particular way as long as it does not affect other portions of the compound; preferred examples are metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide, calcium hydroxide, barium hydroxide and cesium hydroxide, with sodium hydroxide and potassium hydroxide being particularly preferred.

The reaction temperature is typically in the range of 0°C - 100°C, preferably 50°C - 100°C.

The reaction time which varies with the reaction temperature and the like is typically in the range of 10

minutes - 48 hours, preferably 5 hours - 48 hours.

Step C3 is for producing compound (24) and implemented by reacting compound (23) or reactive derivatives thereof (acid halides, mixed acid anhydrides or active esters) with
5 compound (138) or acid addition salts thereof in an inert solvent.

The reaction is performed by, for example, the acid halide method, the mixed acid anhydride method, the active ester method or the condensation method. The acid halide
10 method is implemented by reacting compound (23) with a halogenating agent (e.g. thionyl chloride, chloride oxalate, phosphorus pentachloride, etc.) in an inert solvent to prepare an acid halide which is then reacted with compound (138) or an acid addition salt in an inert solvent in the
15 presence or absence of a base (preferably in it's presence). The base to be used may be exemplified by organic amines such as triethylamine, N-methylmorpholine, pyridine and 4-dimethylaminopyridine, alkali metal bicarbonates such as sodium bicarbonate and potassium bicarbonate, and alkali
20 metal carbonates such as sodium carbonate and potassium carbonate; organic amines are preferred (with triethylamine being particularly preferred).

The solvent to be used is not limited in any particular way as long as it does not participate in the
25 reaction; examples include hydrocarbon solvents such as hexane, cyclohexane, benzene, toluene and xylene, halogen-containing solvents such as dichloromethane, 1,2-dichloroethane and carbon tetrachloride, ether solvents

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such as ether, tetrahydrofuran and dioxane, ketonic solvents such as acetone, amide-containing solvents such as N,N-dimethylacetamide, N,N-dimethylformamide and N-methyl-2-pyrrolidone, and sulfoxide-containing solvents such as dimethyl sulfoxide; preferred examples are hydrocarbon solvents, halogen-containing solvents and ether solvents, and more preferred examples are ether solvents (with tetrahydrofuran being particularly preferred). The reaction temperature varies with the type of solvent and the like; however, for both the reaction of a halogenating agent with compound (23) and the reaction of an acid halide with compound (138) or its acid addition salt, the range is typically between -20 °C and 150 °C; preferably, the temperature for the reaction between a halogenating agent and compound (23) is in the range of -10°C ~ 50°C, and the temperature for the reaction between an acid halide and compound (138) or its acid addition salt is in the range of 0°C - 100°C. The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably, 30 minutes - 15 hours).

The mixed acid anhydride method is implemented by reacting a C₁-C₆ alkyl halogenocarbonate (where C₁-C₆ refers to a straight-chained or branched alkyl group having 1 - 6 carbon atoms), a di-C₁-C₆ alkylcyanophosphoric acid or a diarylphosphorylazide with compound (23) to prepare a mixed acid anhydride which is then reacted with compound (138) or an acid addition salt thereof. The reaction for preparing

a mixed acid anhydride is performed by reacting a C_1-C_6 alkyl halogenocarbonate such as methyl chlorocarbonate, ethyl chlorocarbonate, isobutyl chlorocarbonate or hexyl chlorocarbonate (preferably ethyl chlorocarbonate or isobutyl chlorocarbonate), a di- C_1-C_6 alkylcyanophosphoric acid such as dimethylcyanophosphoric acid, diethylcyanophosphoric acid or dihexylcyanophosphoric acid or a diarylphosphoric acid azide such as diphenylphosphoric acid azide, di-(p-nitrophenyl)phosphoric acid azide or dinaphthylphosphoric acid azide (preferably diphenylphosphoric acid azide) with compound (23), preferably in an inert solvent in the presence of a base.

The base and the inert solvent to be used are the same as those used when the acid halide method is employed in the step under consideration. The reaction temperature which varies with the type of solvent and the like is typically in the range of $-20^{\circ}\text{C} \sim 50^{\circ}\text{C}$ (preferably $0^{\circ}\text{C} - 30^{\circ}\text{C}$). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 15 hours).

The reaction between a mixed acid anhydride and compound (138) or its acid addition salt is performed in an inert solvent in the presence or absence (preferably the presence) of a base, and the base and the inert solvent to be used are the same as those used in the above acid halide method. The reaction temperature which varies with the type of solvent and the like is typically in the range of $-20^{\circ}\text{C} \sim 50^{\circ}\text{C}$ (preferably $0^{\circ}\text{C} - 30^{\circ}\text{C}$). The reaction time

which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 15 hours). If a di-C₁-C₆ alkylcyanophosphoric acid or a diarylphosphoric acid azide is used in the process under consideration, compound (23) may be directly reacted with compound (138) or its acid addition salt in the presence of a base.

The active esterification method is implemented by reacting compound (23) with an active esterifying agent (e.g. N-hydroxy compounds such as N-hydroxysuccinimide and N-hydroxybenzotriazole) in the presence of a condensing agent (e.g. dicyclohexylcarbodiimide or carbonyldiimidazole) to prepare an active ester which is then reacted with compound (138) or an acid addition salt thereof. The reaction for preparing an active ester is preferably performed in an inert solvent and the inert solvent to be used may be exemplified by ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, as well as dimethylformamide, ethyl acetate, acetonitrile, etc.; preferred examples are dichloromethane, acetonitrile, ethyl acetate, etc. The reaction temperature varies with the type of solvent and the like; the temperature for the active esterification reaction is typically in the range of -20°C ~ 50°C (preferably -10°C ~ 30°C), and the temperature for the reaction between the active ester compound and compound (138) or its acid addition salt is typically in

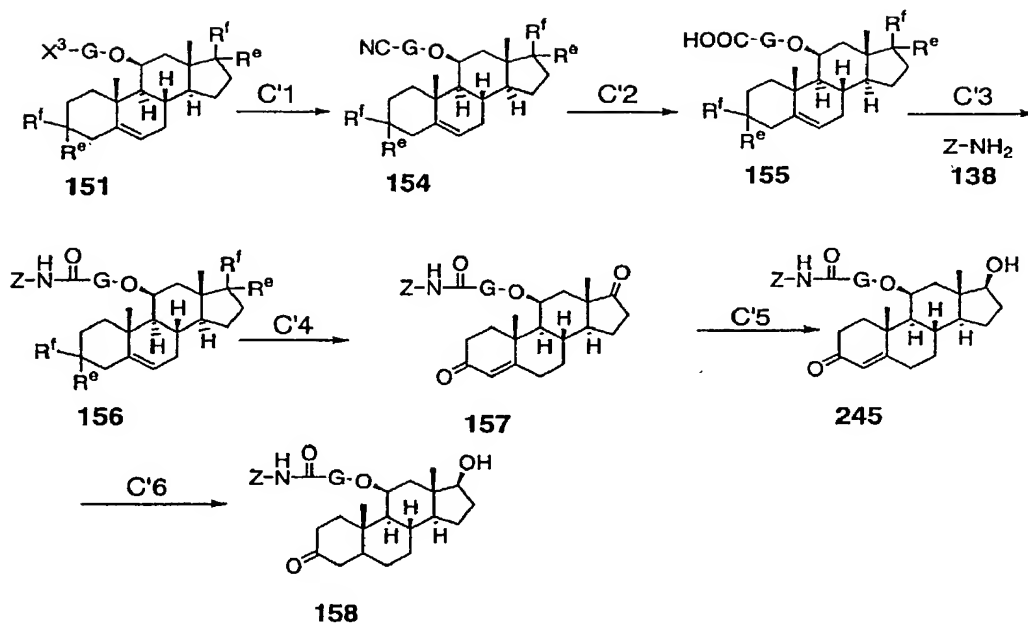
the range of -20°C ~ 50°C (preferably -10°C ~ 30°C). The reaction time varies with the reaction temperature and the like; however, for both reactions, it is typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 15
5 hours).

The condensation method is performed by directly reacting compound (23) with compound (138) or an acid addition salt thereof in the presence of a condensing agent [e.g. dicyclohexylcarbodiimide, carbonyldiimidazole, or 1-
10 (N,N-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride]. This reaction is performed as in the aforementioned reaction for preparing the active ester.

Step C4 is for producing compound (25) and implemented by reacting compound (24) with an acid in an aqueous
15 solvent and this reaction is performed as in the aforementioned step A5 in process A.

Process C' is a method of producing compound (245) having the dashed line in compound (25) forming a double bond together with the solid line, and compound (158)
20 having the dashed line in compound (25) forming a single bond together with the solid line.

Process C'



Step C'1 is for producing compound (154) and implemented by reacting compound (151) with a cyanylating agent in an inert solvent. The reaction is performed as in the aforementioned step C1 in process C.

Step C'2 is for producing compound (155) and implemented by hydrolyzing compound (154) in the presence of a base. The reaction is performed as in the aforementioned step C2 in process C.

Step c'3 is for producing compound (156) and implemented by reacting compound (155) or reactive derivatives thereof (acid halides, mixed acid anhydrides or active esters) with compound (138) or acid addition salts thereof in an inert solvent. The reaction is performed as in the aforementioned step C3 in process C.

Step C'4 is for producing compound (157) and implemented by reacting compound (156) with an acid in an

The condition to be used in catalytic reduction is a homogeneous system such as hydrogen-chlorotris(triphenylphosphine)rhodium(I), hydrogen-chlorotris(triparatolyphosphine)rhodium(I), hydrogen-5 chlorotris(triparamethoxyphenylphosphine)rhodium(I), hydrogen-hydridecarbonyltris(triphenylphosphine)rhodium(I), hydrogen-rhodium(II) acetate, hydrogen-ruthenium(II) acetate, hydrogen-chlorohydridetris(triphenylphosphine)ruthenium(II), 10 hydrogen-carboxylatohydridetris(triphenylphosphine)ruthenium(II), hydrogen-hydridecarbonyltris(triphenylphosphine)iridium(I), hydrogen-platinum(II)-tin chloride complex, hydrogen-pentacyanocobalt(II) complex, hydrogen-tricyanobipyridine 15 cobalt(II) complex, hydrogen-bis(dimethylglyoximato)cobalt(II) complex, hydrogen-methyl benzoate-tricarbonylchromium complex, hydrogen-bis(tricarbonylcyclopentadienylchromium), hydrogen-pentacarbonyliron, hydrogen-20 bis(cyclopentadienyl)dicarbonyltitanium, hydrogen-hydridecarbonylcobalt complex, hydrogen-octacarbonyldicobalt, hydrogen-hydridecarbonylrhodium, hydrogen-chromium(III) acetylacetonato-triisobutylaluminum, hydrogen-cobalt(II) acetylacetonato-triisobutylaluminum, or 25 hydrogen-nickel(II)-2-hexanoato-triethylaluminum, or an inhomogeneous system condition such as hydrogen-platinum dioxide, hydrogen-platinum/carbon, hydrogen-palladium/carbon, hydrogen-palladium/barium sulfate,

hydrogen-palladium/calcium carbonate, hydrogen-Raney nickel,
hydrogen-copper chromite, hydrogen-rhodium/carbon,
hydrogen-rhodium/alumina, hydrogen-ruthenium dioxide, or
hydrogen-ruthenium/carbon; preferred examples are hydrogen-
5 chlorotris(triphenylphosphine)rhodium(I), hydrogen-
palladium/carbon, hydrogen-palladium/calcium carbonate, etc.

The reaction temperature is typically in the range of
0°C - 100°C, preferably 0°C - 60°C. The reaction time which
varies with the reaction temperature and the like is
10 typically in the range of 10 minutes - 24 hours, preferably
10 minutes - 6 hours.

The inert solvent to be used in the reaction with the
reducing agent is not limited in any particular way as long
as it does not participate in the reaction; examples
15 include ether solvents such as ether, tetrahydrofuran,
dioxane and dimethoxyethane, aromatic solvents such as
benzene, toluene, xylene, quinoline and chlorobenzene,
halogen-containing solvents such as dichloromethane,
chloroform and carbon tetrachloride, amine-containing
20 solvents such as pyridine and triethylamine, as well as
cyclohexane, dimethyl sulfoxide, dimethylacetamide,
dimethylimidazolidinone, dimethylformamide, N-
methylpyrrolidone, acetonitrile and nitromethane; preferred
examples are tetrahydrofuran, benzene, toluene and pyridine.

25 The reducing agent to be used may be exemplified by
metals such as sodium/liquid ammonia, lithium/liquid
ammonia, lithium/methylamine, lithium/ethylamine,
lithium/ethylenediamine, sodium/hexamethylphosphamide-t-

butanol, sodium/ethanol, sodium/t-butanol-tetrahydrofuran, sodium/toluene-t-amyl alcohol, metal hydrides such as triphenyltin hydride, tri-n-butyltin hydride, diphenyltin hydride, di-n-butyltin hydride, triethyltin hydride, 5 trimethyltin hydride, trichlorosilane/tri-n-butylamine, trichlorosilane/tri-n-propylamine, triethylsilane, trimethylsilane, diphenylsilane, phenylsilane, polymethylhydrosiloxane, dimethylphenylsilane, di-n-butylsilane and methylphenylsilane; metal hydrogen complex 10 compounds such as lithium aluminum hydride/copper(I) iodide, trimethoxyaluminum lithium hydride/copper(I) bromide, tri-t-butoxyaluminum lithium hydride/copper(I) bromide, sodium boron hydride, sodium boron hydride-palladium/carbon, sodium boron hydrogensulfide, sodium boron hydrogencyanide, 15 sodium trimethoxyboron hydride, lithium boron hydride, lithium boron hydrogencyanide, lithium triethylboron hydride, lithium tri-s-butylboron hydride, lithium tri-t-butylboron hydride, calcium boron hydride, potassium boron hydride, potassium triisopropoxyboron hydride, potassium 20 tri-s-butylboron hydride, zinc boron hydride, tetramethylammonium boron hydride and tetra-n-butylammonium cyanoboron hydride; preferred examples are sodium/liquid ammonia, lithium/liquid ammonia, triphenyltin hydride, tri-n-butyltin hydride, lithium aluminum hydride/copper(I) 25 iodide, trimethoxyaluminum lithium hydride/copper(I) bromide, sodium boron hydride and potassium tri-s-butylboron hydride.

The reaction temperature which varies with the type of

by reacting compound (14) with phthalimide in an inert solvent in the presence of an azodicarboxylic acid dialkyl ester (preferably diethyl azodicarboxylate) and a phosphine compound (preferably triphenylphosphine).

5 The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction; examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, and aromatic solvents such as benzene, toluene, xylene, quinoline and
10 chlorobenzene, with tetrahydrofuran being preferred. The reaction temperature which varies with the type of solvent and the like is typically in the range of 0°C - 50°C (preferably 10°C - 30°C). The reaction time which varies with the reaction temperature and the like is typically in
15 the range of 15 minutes - 48 hours (preferably 30 minutes - 24 hours).

Step D2 is an alternative step for producing compound (27) and implemented by reacting compound (15) with a metal salt of phthalimide (preferably phthalimide potassium) in
20 an inert solvent.

The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction; examples include ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, aromatic
25 solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, halogen-containing solvents such as dichloromethane, as well as dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone,

dimethylformamide, and N-methylpyrrolidone; a preferred example is tetrahydrofuran.

The reaction temperature which varies with the type of solvent and the like is typically in the range of 0°C - 50°C (preferably 10°C - 30°C). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 48 hours (preferably 30 minutes - 24 hours).

Step D3 is for producing compound (28) and implemented by reacting compound (27) with an amine-containing compound (preferably hydrazine) in an alcoholic solvent.

The alcoholic solvent to be used is not limited in any particular way as long as it does not interfere with the reaction and examples are methanol, ethanol, n-propyl alcohol and i-propyl alcohol, with ethanol being preferred.

The reaction temperature which varies with the type of solvent and the like is typically in the range of 0°C - 50°C (preferably 10°C - 30°C). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 48 hours (preferably 30 minutes - 24 hours).

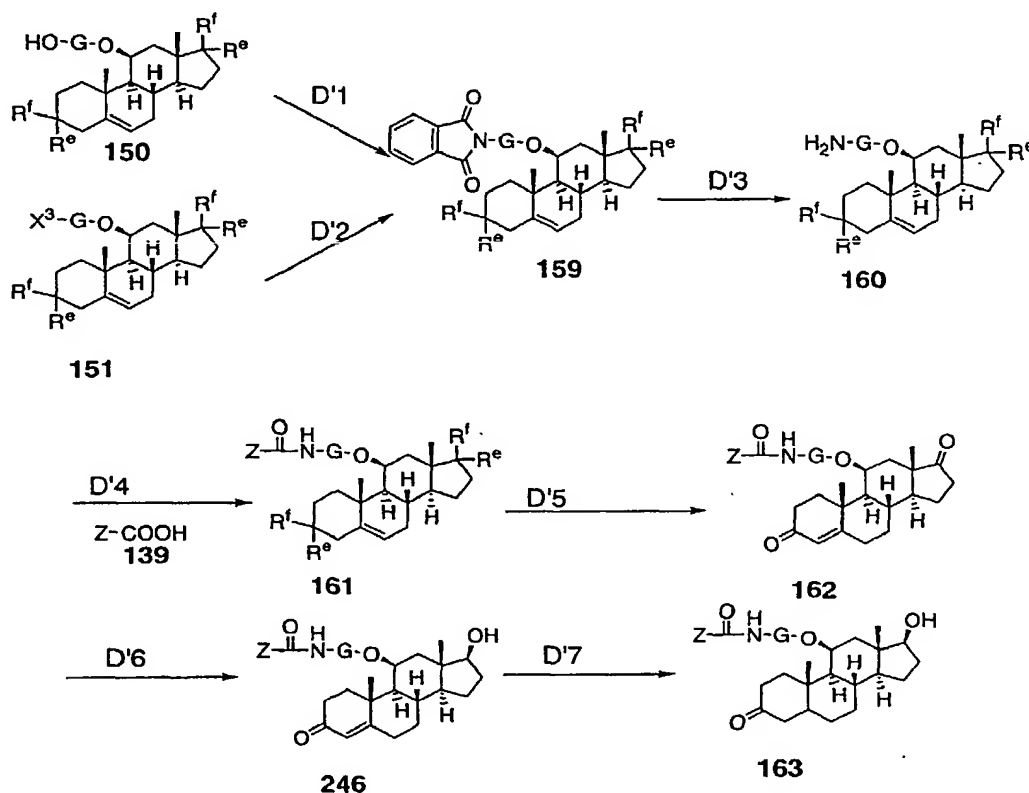
Step D4 is for producing compound (29) and implemented by reacting compound (139) or reactive derivatives thereof (acid halides, mixed acid anhydrides or active esters) with compound (28) or acid addition salts thereof in an inert solvent. The reaction is performed as in the aforementioned step C3 in process C.

Step D5 is for producing compound (30) and implemented

by reacting compound (29) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step A5 in process A.

Process D' is a method of producing compound (246) having the dashed line in compound (30) forming a double bond together with the solid line, and compound (163) having the dashed line in compound (30) forming a single bond together with the solid line.

Process D'



10

Step D'1 is for producing compound (159) and implemented by reacting compound (150) with phthalimide in an inert solvent in the presence of an azodicarboxylic acid dialkyl ester (preferably diethyl azodicarboxylate) and a

phosphine compound (preferably triphenylphosphine). The reaction is performed as in the aforementioned step D1 in process D.

Step D'2 is an alternative step for producing compound
5 (159) and implemented by reacting compound (151) with a metal salt of phthalimide (preferably phthalimide potassium) in an inert solvent. The reaction is performed as in the aforementioned step D2 in process D.

Step D'3 is for producing compound (160) and
10 implemented by reacting compound (159) with an amine-containing compound (preferably hydrazine) in an alcoholic solvent. The reaction is performed as in the aforementioned step D3 in process D.

Step D'4 is for producing compound (161) and
15 implemented by reacting compound (139) or reactive derivatives thereof (acid halides, mixed acid anhydrides or active esters) with compound (160) or acid addition salts thereof in an inert solvent. The reaction is performed as in the aforementioned step D4 in process D.

Step D'5 is for producing compound (162) and
20 implemented by reacting compound (161) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step C4 in process C.

Step D'6 is for producing compound (246) and
25 implemented by reacting compound (162) with a reducing agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step A12 in process A.

Step D'7 is for producing compound (163) and implemented by performing catalytic reduction of compound (246) in an alcoholic solvent or an inert solvent or by reacting compound (246) with a reducing agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step C'6 in process C'.

Process E is for producing compound (35) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}=\text{CH}-\text{CH}_2-\text{R}^4$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond or a double bond; compound (36) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-(\text{CH}_2)_3-\text{R}^4$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})$, and the dashed line together with the solid line is a single bond or a double bond; compound (38) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-(\text{CH}_2)_3-\text{G}^3-\text{S}(\text{O})-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position

Step E1 is for producing compound (32) and implemented by reacting compound (134) with a metal (preferably magnesium) or an alkyllithium (preferably t-butyllithium) in an inert solvent to make a reactive derivative of compound (134) and reacting it with compound (2) in an inert solvent. The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction; preferred examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, and tetrahydrofuran is more preferred.

The reaction temperature which varies with the type of solvent and the like is typically in the range of 0°C - 80°C (preferably 10°C - 50°C). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 15 hours).

The reaction of interest can also be implemented by reacting compound (2) with compound (140) in an inert solvent in the presence of an activator.

The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction; preferred examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, and halogen-containing solvents such as dichloromethane; more preferred examples are tetrahydrofuran and dichloromethane.

The activator to be used is not limited in any particular way as long as it does not interfere with the reaction; examples are fluorides such as tetra-n-

butylammonium fluoride, and Lewis acids such as aluminum trichloride, ethylaluminum dichloride, titanium tetrachloride, boron trifluoride, and trimethylsilyl trifluoromethanesulfonate; a preferred example is

5 trimethylsilyl trifluoromethanesulfonate.

The reaction temperature which varies with the type of solvent and the like is typically in the range of -78°C ~ 50°C (preferably -60°C ~ 30°C). The reaction time which varies with the reaction temperature and the like is

10 typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 5 hours).

Step E2 is for producing compound (33) and implemented by reacting compound (32) with a reducing agent in an inert solvent in the presence of an additive.

15 The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction; examples include aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, halogen-containing solvents such as dichloromethane,

20 chloroform and carbon tetrachloride, and ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane; preferred examples are benzene, toluene and dichloromethane.

The additive to be used is not limited in any

25 particular way as long as it does not interfere with the reaction and preferred examples are 1,1'-thiocarbonyl diimidazole, phosgene, benzoyl chloride, zinc iodide, boron trifluoride (BF_3), etc.

The reducing agent to be used may be exemplified by metal hydrides such as triphenyltin hydride, tri-n-butyltin hydride, diphenyltin hydride, di-n-butyltin hydride, triethyltin hydride, trimethyltin hydride,

5 trichlorosilane/tri-n-butylamine, trichlorosilane/tri-n-propylamine, triethylsilane, trimethylsilane, diphenylsilane, phenylsilane, polymethylhydrosiloxane, dimethylphenylsilane, di-n-butylsilane and methylphenylsilane; and metal hydrogen complex compounds

10 such as lithium aluminum hydride, trimethoxyaluminum lithium hydride, tri-t-butoxyaluminum lithium hydride, lithium aluminum hydride-trichloroaluminum (alane), lithium aluminum hydride-boron trifluoride, aluminum hydride magnesium chloride, magnesium aluminum hydride, sodium

15 aluminum hydride, sodium triethoxyaluminum hydride, sodium bis(methoxyethoxy)aluminum hydride, sodium boron hydride, sodium boron hydride-palladium/carbon, sodium boron hydrogensulfide, sodium boron hydrogencyanide, sodium trimethoxyboron hydride, lithium boron hydride, lithium

20 boron hydrogencyanide, lithium triethylboron hydride, lithium tri-s-butylboron hydride, lithium tri-t-butylboron hydride, calcium boron hydride, potassium boron hydride, potassium triisopropoxyboron hydride, potassium tri-s-butylboron hydride, zinc boron hydride, tetramethylammonium

25 boron hydride, and tetra-n-butylammonium cyanoboron hydride; preferred examples are tri-n-butyltin hydride, triethylsilane and sodium boron hydrogencyanide.

The reaction temperature which varies with the type of

solvent and the like is typically in the range of 0°C ~ 150°C (preferably 10°C ~ 100°C). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 15 hours).

In this step, a compound having the allyl group in the 11-position of compound (33) oriented in α configuration forms as a by-product and this may be used to give compounds having X^1 in compound (35), compound (36), compound (38) and compound (39) oriented in α configuration.

Step E3 is for producing compound (34) and implemented by reacting compound (33) with compound (141) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the aforementioned step A4 in process A.

Step E4 is for producing compound (35) and implemented by reacting compound (34) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step A5 in process A.

20 Step E5 is for producing compound (36) and implemented
by performing catalytic reduction in an alcoholic solvent
or an inert solvent. The reaction is performed as in the
aforementioned step A6 in process A.

Step E7 is for producing compound (38) in the case
25 where Q² in R⁴ in compound (36) is -S- and implemented by
reacting compound (36) with an oxidizing agent in an inert
solvent. The reaction is performed as in the
aforementioned step A8 in process A.

(164) in an inert solvent. Alternatively, step E'1 may be implemented by reacting compound (164) with compound (140) in an inert solvent in the presence of an activator. The reaction is performed as in the aforementioned step E1 in
5 process E.

Step E'2 is for producing compound (166) and implemented by reacting compound (166) with a reducing agent in an inert solvent in the presence of an additive. The reaction is performed as in the aforementioned step E2
10 in process E.

In this step, a compound having the allyl group in the 11-position of compound (166) oriented in α configuration forms as a by-product and this may be used to give compounds having X^1 in compound (35) and compound (36)
15 oriented in α configuration.

Step E'3 is for producing compound (167) and implemented by reacting compound (166) with compound (141) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the
20 aforementioned step E3 in process E.

Step E'4 is for producing compound (168) and implemented by reacting compound (167) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step D'5 in process D'.

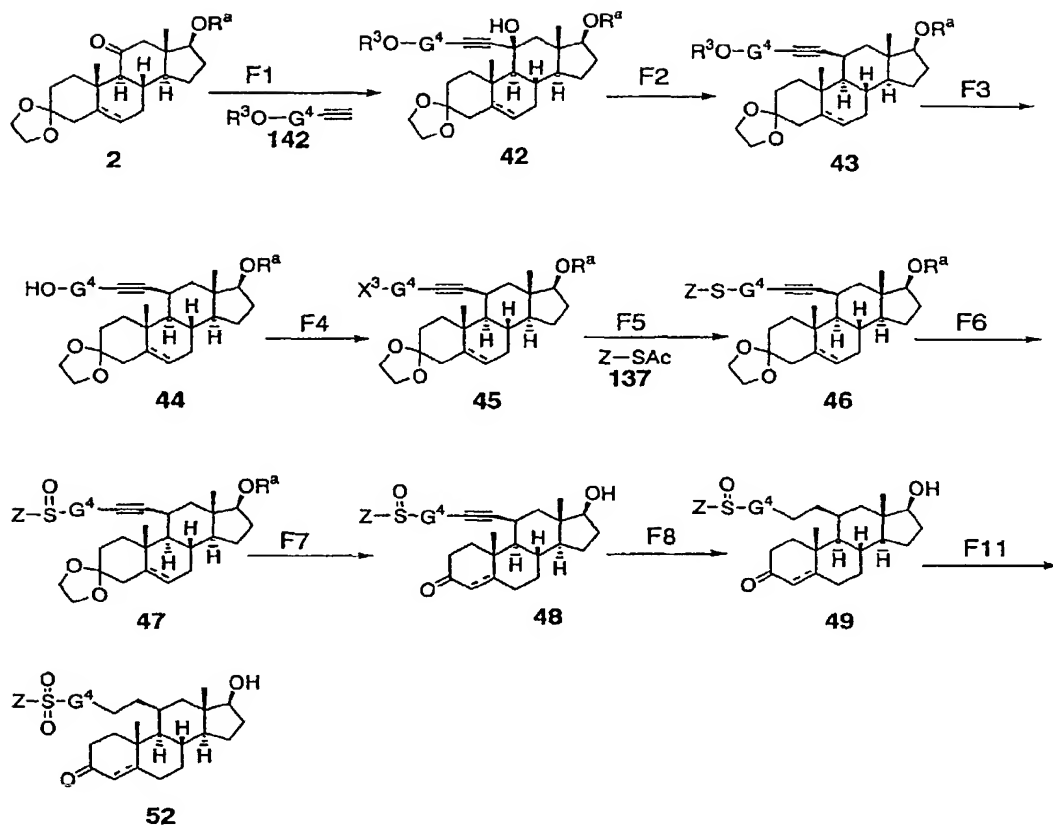
25 Step E'5 is for producing compound (247) and implemented by reacting compound (168) with a reducing agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step A12 in

process A.

Step E'6 is for producing compound (36) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step A6 in process A.

Process F is for producing compound (49) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{G}^4-\text{S}(\text{O})-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond or a double bond, and compound (52) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{G}^4-\text{S}(\text{O})_2-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond or a double bond.

Process F



Step F1 is for producing compound (42) and implemented by reacting compound (142) with an alkyl lithium (preferably n-butyllithium) in an inert solvent to make a reactive derivative of compound (142) and reacting it with compound (2) in an inert solvent.

The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction; preferred examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, and tetrahydrofuran is more preferred.

The reaction temperature which varies with the type of solvent and the like is typically in the range of 0 °C - 80

solvent. The reaction is performed as in the
aforementioned step B4 in process B.

Step F6 is for producing compound (47) and implemented
by reacting compound (46) with an oxidizing agent in an
5 inert solvent. The reaction is performed as in the
aforementioned step A8 in process A.

Step F7 is for producing compound (48) and implemented
by reacting compound (47) with an acid in an aqueous
solvent. The reaction is performed as in the
10 aforementioned step A5 in process A.

Step F8 is for producing compound (49) and implemented
by performing catalytic reduction of compound (48) in an
alcoholic solvent or an inert solvent.

The solvent to be used may be exemplified by alcoholic
15 solvents such as methanol, ethanol, n-propanol, i-propanol,
n-butanol, s-butanol, t-butanol, pentanol, hexanol,
cyclopropanol, cyclobutanol, cyclopentanol, cyclohexanol,
ethylene glycol, 1,3-propanediol, 1,4-butanediol, and 1,5-
pentanediol, ether solvents such as ether, tetrahydrofuran,
20 dioxane and dimethoxyethane, aromatic solvents such as
benzene, toluene, xylene, quinoline and chlorobenzene,
halogen-containing solvents such as dichloromethane,
chloroform and carbon tetrachloride, as well as cyclohexane,
dimethyl sulfoxide, dimethylacetamide,
25 dimethylimidazolidinone, dimethylformamide, N-
methylpyrrolidone, ethyl acetate, acetonitrile and
nitromethane; a preferred example is ethyl acetate.

The condition to be used in catalytic reduction is a

- homogeneous system such as hydrogen-chlorotris(triphenylphosphine)rhodium(I), hydrogen-chlorotris(triparatolylphosphine)rhodium(I), hydrogen-chlorotris(triparamethoxyphenylphosphine)rhodium(I),
- 5 hydrogen-hydridecarbonyltris(triphenylphosphine)rhodium(I), hydrogen-rhodium(II) acetate, hydrogen-ruthenium(II) acetate, hydrogen-chlorohydridetris(triphenylphosphine)ruthenium(II), hydrogen-
- 10 carboxylatohydridetris(triphenylphosphine)ruthenium(II), hydrogen-hydridecarbonyltris(triphenylphosphine)iridium(I), hydrogen-platinum(II)-tin chloride complex, hydrogen-pentacyanocobalt(II) complex, hydrogen-tricyanobipyridine cobalt(II) complex, hydrogen-
- 15 bis(dimethylglyoximato)cobalt(II) complex, hydrogen-methyl benzoate-tricarbonylchromium complex, hydrogen-bis(tricarbonylcyclopentadienylchromium), hydrogen-pentacarbonyliron, hydrogen-bis(cyclopentadienyl)dicarbonyltitanium, hydrogen-
- 20 hydridecarbonylcobalt complex, hydrogen-octacarbonyldicobalt, hydrogen-hydridecarbonylrhodium, hydrogen-chromium(III) acetylacetonato-triisobutylaluminum, hydrogen-cobalt(II) acetylacetonato-triisobutylaluminum, or hydrogen-nickel(II)-2-hexanoato-triethylaluminum, or an
- 25 inhomogeneous system condition such as hydrogen-platinum dioxide, hydrogen-platinum/carbon, hydrogen-palladium/carbon, hydrogen-palladium/barium sulfate, hydrogen-palladium/calcium carbonate, hydrogen-Raney nickel,

hydrogen-copper chromite, hydrogen-rhodium/carbon, hydrogen-rhodium/alumina, hydrogen-ruthenium dioxide, or hydrogen-ruthenium/carbon; a preferred example is hydrogen palladium/carbon.

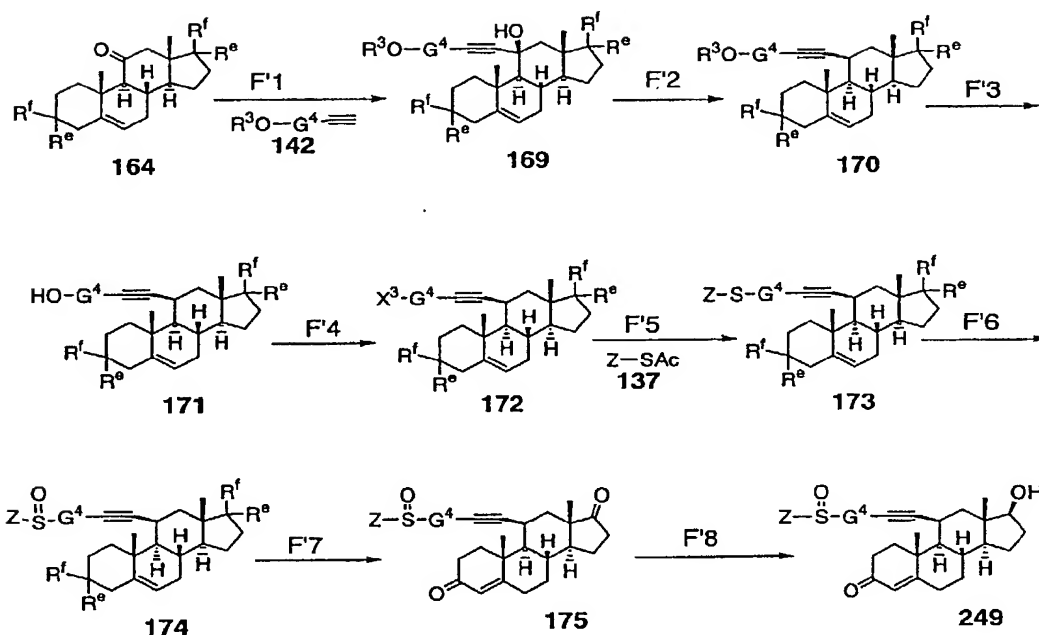
5 The reaction temperature is typically in the range of 0°C - 100°C, preferably 0°C - 60°C. The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 24 hours, preferably 10 minutes - 6 hours.

10 As an ancillary to this reaction, conversion to a single bond may occasionally be effected if the dashed line forms a double bond together with the solid line.

Step F11 is for producing compound (52) and implemented by reacting compound (49) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step B7 in process B.

Process F' is an alternative method of producing compound (249) having the dashed line in compound (48) forming a double bond together with the solid line.

20 Process F'



Step F'1 is for producing compound (169) and implemented by reacting compound (142) with an alkyl lithium (preferably n-butyllithium) in an inert solvent to make a reactive derivative of compound (142) and reacting it with compound (164) in an inert solvent. The reaction is performed as in the aforementioned step F1 in process F.

Step F'2 is for producing compound (170) and
10 implemented by reacting compound (169) with a reducing
agent in an inert solvent in the presence of an additive.
The reaction is performed as in the aforementioned step F2
in process F.

In this step, a compound having the substituent in the
15 11-position of compound (170) oriented in α configuration
forms as a by-product and this may be used to give a
compound having X¹ in compound (249) oriented in α

agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step E'5 in process E.

Process G is for producing compound (56) represented
5 by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{G}^4-\text{COOH}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the
10 carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond or a double bond, and compound (57) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general
15 formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{G}^4-\text{CONH}-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is
20 a single bond or a double bond.

Process G

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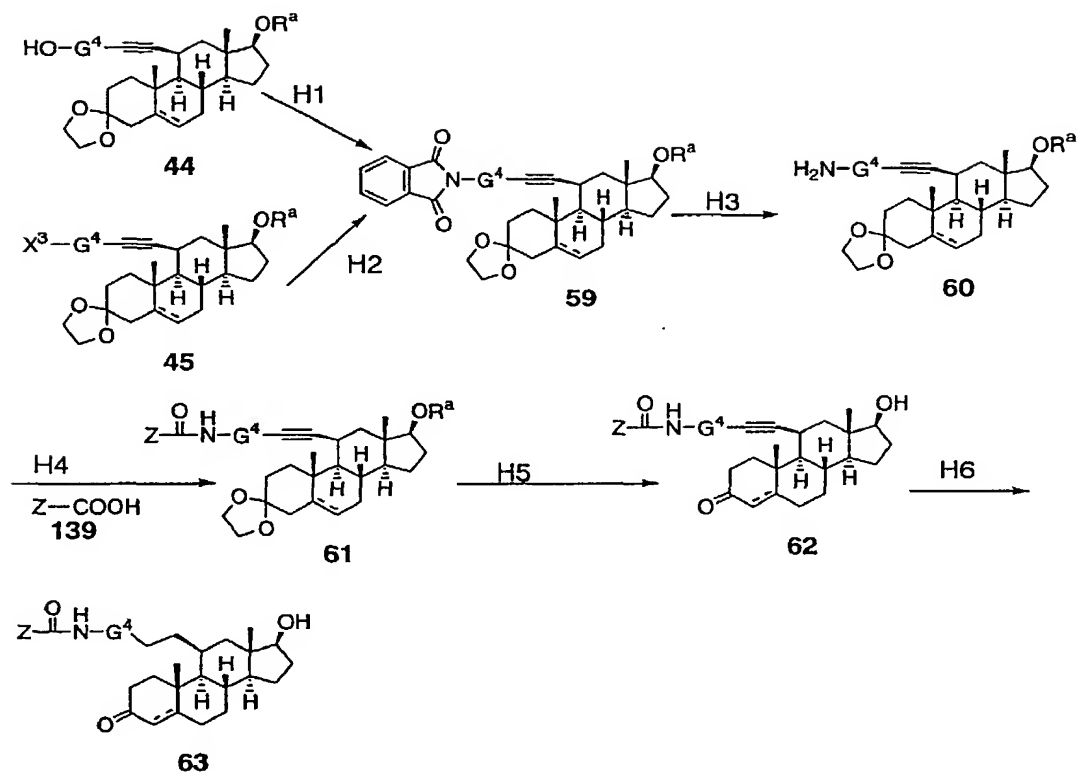
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implemented by reacting compound (177) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step F'7 in process F'.

Step G'4 is for producing compound (250) and
5 implemented by reacting compound (178) with a reducing agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step F'8 in process F'.

Process H is for producing compound (63) represented by the general formula (I) in which X^1 is a group of β
10 configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{G}^4-\text{NHCO}-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are
15 $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond or a double bond.

Process H



Step H1 is for producing compound (59) and implemented by reacting compound (44) with phthalimide in an inert solvent in the presence of an azodicarboxylic acid dialkyl ester (preferably diethyl azodicarboxylate) and a phosphine compound (preferably triphenylphosphine). The reaction is performed as in the aforementioned step D1 in process D.

Step H2 is an alternative step for producing compound (59) and implemented by reacting compound (45) with a metal salt of phthalimide (preferably phthalimide potassium) in an inert solvent. The reaction is performed as in the aforementioned step D2 in process D.

Step H3 is for producing compound (60) and implemented by reacting compound (59) with an amine-containing compound

(preferably hydrazine) in an alcoholic solvent. The reaction is performed as in the aforementioned step D3 in process D.

5 Step H4 is for producing compound (61) and implemented by reacting compound (139) or reactive derivatives thereof (acid halides, mixed acid anhydrides or active esters) with compound (60) or acid addition salts thereof in an inert solvent. The reaction is performed as in the aforementioned step C3 in process C.

10 Step H5 is for producing compound (62) and implemented by reacting compound (61) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step A5 in process A.

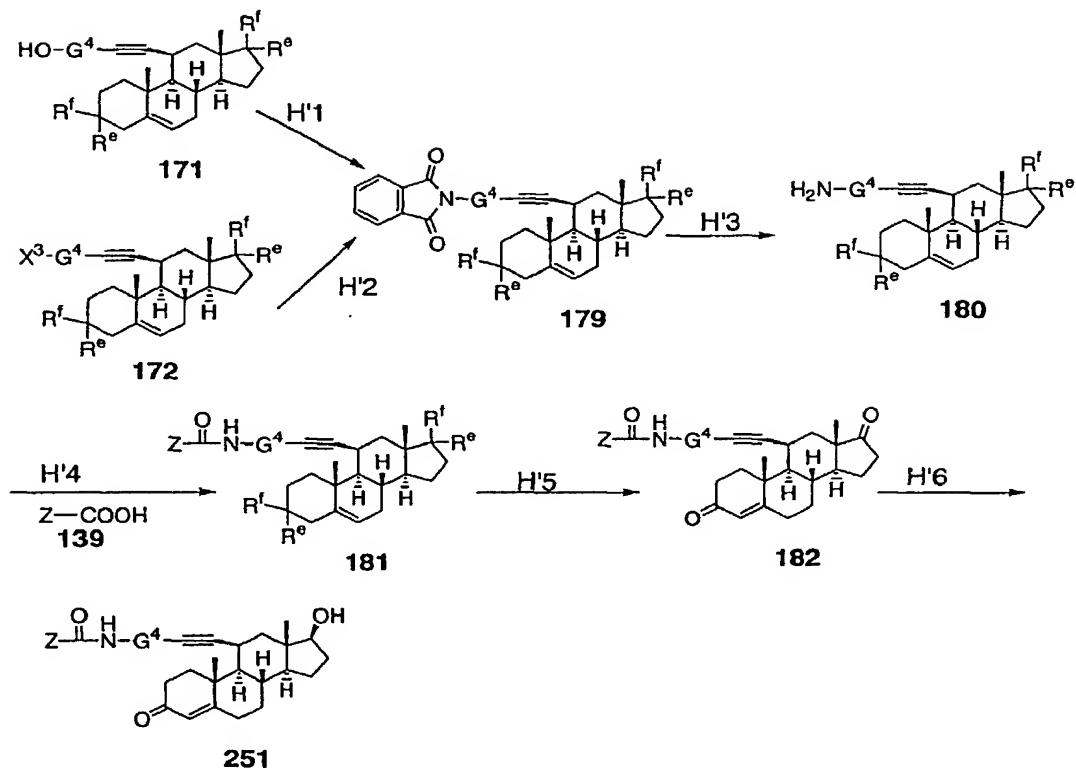
15 Step H6 is for producing compound (63) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step F8 in process F.

20 As an ancillary to this reaction, conversion to a single bond may occasionally be effected if the dashed line forms a double bond together with the solid line.

Process H' is an alternative method of producing compound (251) having the dashed line in compound (62) forming a double bond together with the solid line.

Process H'

25



Step H'1 is for producing compound (179) and implemented by reacting compound (171) with phthalimide in an inert solvent in the presence of an azodicarboxylic acid dialkyl ester (preferably diethyl azodicarboxylate) and a phosphine compound (preferably triphenylphosphine). The reaction is performed as in the aforementioned step H1 in process H.

Step H'2 is an alternative step for producing compound (179) and implemented by reacting compound (172) with a metal salt of phthalimide (preferably phthalimide potassium) in an inert solvent. The reaction is performed as in the aforementioned step H2 in process H.

Step H'3 is for producing compound (180) and

5 Step H'4 is for producing compound (181) and
implemented by reacting compound (139) or reactive
derivatives thereof (acid halides, mixed acid anhydrides or
active esters) with compound (180) or acid addition salts
thereof in an inert solvent. The reaction is performed as
10 in the aforementioned step H4 in process H.

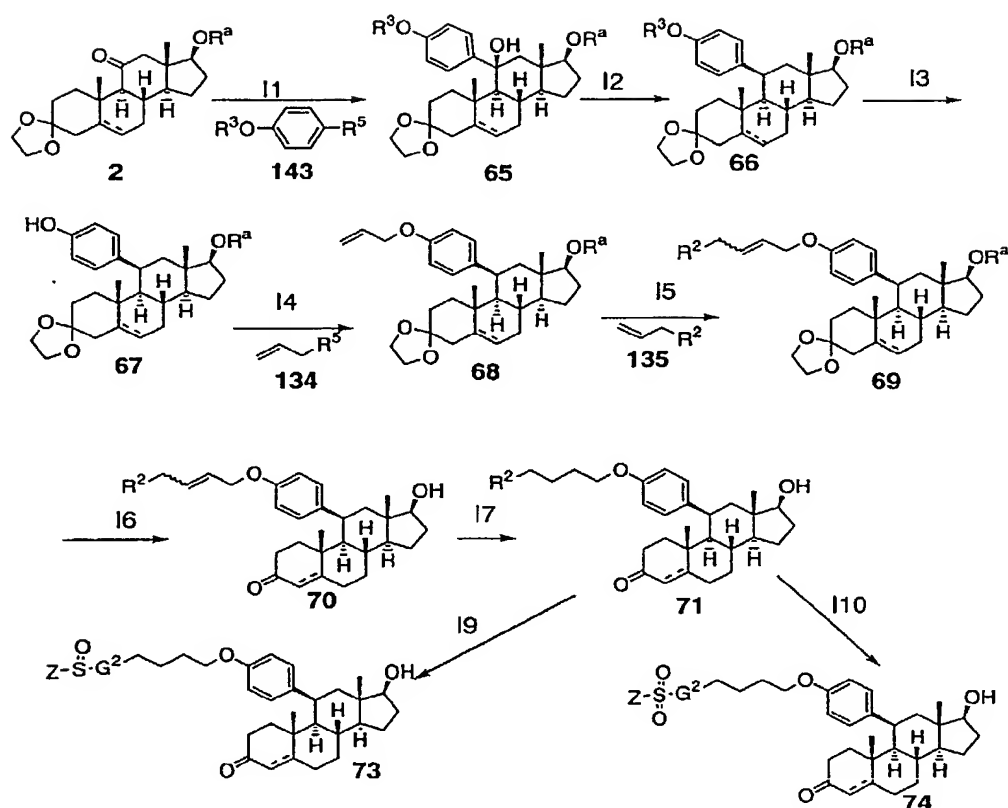
Step H'5 is for producing compound (182) and implemented by reacting compound (181) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step G'3 in process G'.

15 Step H'6 is for producing compound (251) and
implemented by reacting compound (182) with a reducing
agent in an optionally miscible inert solvent. The
reaction is performed as in the aforementioned step G'4 in
process G'.

20 Process I is for producing compound (70) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is -CH₂-
25 CH=CH-CH₂-R², X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond

or a double bond; compound (71) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is $-(CH_2)_4-R^2$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)$, and the dashed line together with the solid line is a single bond or a double bond; compound (73) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is $-(CH_2)_4-G^2-S(O)-Z$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond; and compound (74) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is $-(CH_2)_4-G^2-S(O)_2-Z$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond.

Process I



Step I1 is for producing compound (65) and implemented by reacting compound (143) with a metal (preferably

5 magnesium) or an alkyl lithium (preferably n-butyllithium) in an inert solvent to make a reactive derivative of compound (143) and reacting it with compound (2) in an inert solvent. The inert solvent to be used is not limited

10 in any particular way as long as it does not participate in the reaction; preferred examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, and tetrahydrofuran is more preferred. The reaction temperature which varies with the type of solvent and the like is typically in the range of 0°C - 80°C (preferably

10°C - 50°C). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 15 hours).

Step I2 is for producing compound (66) and implemented
5 by reacting compound (65) with a reducing agent in an inert solvent in the presence of an additive. The reaction is performed as in the aforementioned step E2 in process E.

In this step, a compound having the $-C_6H_4-OR^3$ in the 11-position of compound (66) oriented in α configuration
10 forms as a by-product and this may be used to give compounds having X^1 in compound (70), compound (71), compound (73) and compound (74) oriented in α configuration.

For the synthesis of compound (66) and a compound having the $-C_6H_4-OR^3$ in the 11-position of compound (66)
15 oriented in α configuration, reference may be had to the methods of introducing a variety of aromatic hydrocarbon groups as disclosed in Tetrahedron, vol. 52, 1529-1542, 1996.

Step I3 is for producing compound (67) and implemented
20 by reacting compound (66) with a deprotecting agent, namely, removing the substituted silyl group, in an inert solvent.

The inert solvent to be used is not limited in an particular way as long as it does not interfere with the reaction; examples include ether solvents such as ether,
25 tetrahydrofuran, dioxane and dimethoxyethane, as well as dimethylformamide and water, with tetrahydrofuran being preferred. The deprotecting agent to be used is not limited in any particular way and may be exemplified by

fluorides such as hydrogen fluoride, hydrogen fluoride-pyridine, sodium fluoride, potassium fluoride and tetra-n-butylammonium fluoride, and organic acids such as formic acid, acetic acid and p-toluenesulfonic acid, with tetra-n-
5 butylammonium fluoride being preferred.

The reaction temperature which varies with the type of solvent and the like is typically in the range of 0°C - 80°C (preferably 0°C - 50°C). The reaction time which varies with the reaction temperature and the like is typically in
10 the range of 15 minutes - 24 hours (preferably 30 minutes - 15 hours).

Step I4 is for producing compound (68) and implemented by reacting compound (67) with a base in an inert solvent to make a salt of compound (67) and then reacting it with
15 compound (134) in an inert solvent. The reaction is performed as in the aforementioned step A3 in process A.

Step I5 is for producing compound (69) and implemented by reacting compound (68) with compound (135) in an inert solvent in the presence of an organometallic catalyst. The
20 reaction is performed as in the aforementioned step A4 in process A.

Step I6 is for producing compound (70) and implemented by reacting compound (69) with an acid in an aqueous solvent. The reaction is performed as in the
25 aforementioned step A5 in process A.

Step I7 is for producing compound (71) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the

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15 Process I'



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implemented by reacting compound (143) with a metal (preferably magnesium) or an alkyllithium (preferably n-butyllithium) in an inert solvent to make a reactive derivative of compound (143) and reacting it with compound
5 (164) in an inert solvent. The reaction is performed as in the aforementioned step I1 in process I.

Step I'2 is for producing compound (185) and implemented by reacting compound (184) with a reducing agent in an inert solvent in the presence of an additive.
10 The reaction is performed as in the aforementioned step I2 in process I.

In this step, a compound having the $-C_6H_4-OR^3$ in the 11-position of compound (185) oriented in α configuration forms as a by-product and this may be used to give a
15 compound having X^1 in compound (252) oriented in α configuration.

For the synthesis of compound (185) and a compound having the $-C_6H_4-OR^3$ in the 11-position of compound (185) oriented in α configuration, reference may be had to the
20 methods of introducing a variety of aromatic hydrocarbon groups as disclosed in Tetrahedron, vol. 52, 1529-1542, 1996.

Step I'3 is for producing compound (186) and implemented by reacting compound (185) with a deprotecting
25 agent, namely, removing the substituted silyl group, in an inert solvent. The reaction is performed as in the aforementioned step I3 in process I.

Step I'4 is for producing compound (187) and

implemented by reacting compound (186) with a base in an inert solvent to make a salt of compound (186) and then reacting it with compound (134) in an inert solvent. The reaction is performed as in the aforementioned step I4 in process I.

Step I'5 is for producing compound (188) and implemented by reacting compound (187) with compound (135) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the aforementioned step I5 in process I.

Step I'6 is for producing compound (189) and implemented by reacting compound (188) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step H'5 in process H'.

Step I'7 is for producing compound (252) and implemented by reacting compound (189) with a reducing agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step H'6 in process H'.

Process J is for producing compound (81) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is -G-S-Z, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond;

compound (82) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -

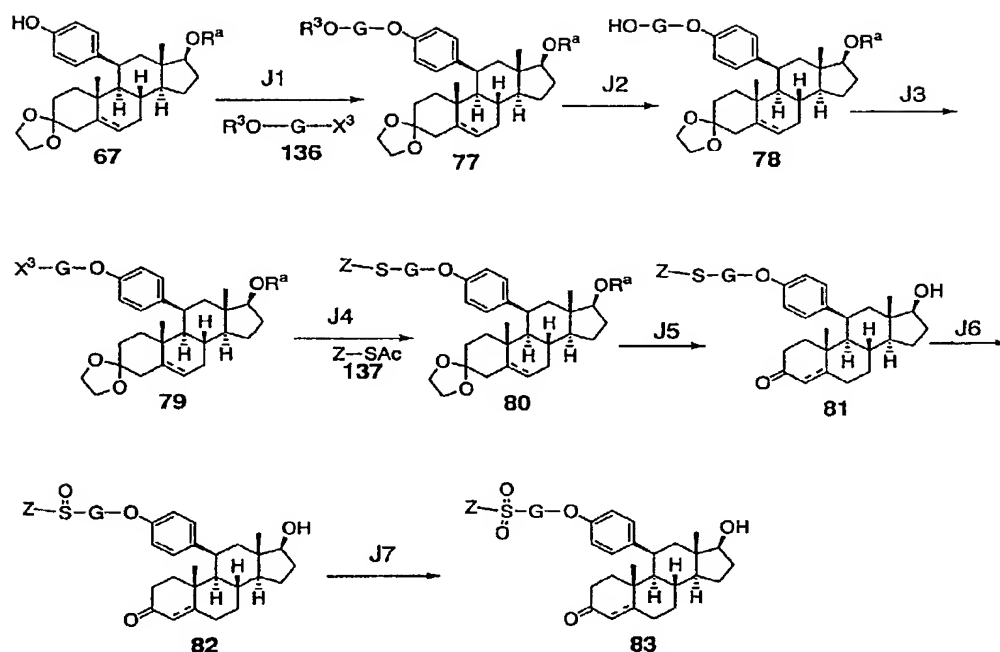
5 O- and R^1 is -G-S(O)-Z, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are - (C=O), and the dashed line together with the solid line is a single bond or a double bond; and compound (83)

10 represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is -G²-S(O)₂-Z, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and

15 R^c , when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond.

Process J

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Step J1 is for producing compound (77) and implemented by reacting compound (67) with a base in an inert solvent to make a salt of compound (67) and reacting it with compound (136) in an inert solvent. The reaction is performed as in the aforementioned step A3 in process A.

Step J2 is for producing compound (78) and implemented by reacting compound (77) with a deprotecting agent, namely, removing the substituted silyl group, in an inert solvent. The reaction is performed as in the aforementioned step B2 in process B.

Step J3 is for producing compound (79) and implemented by reacting compound (78) with a sulfonyl chloride compound in an amine-containing solvent or reacting compound (78) with a halogenating agent in an inert solvent. The reaction is performed as in the aforementioned step B3 in

process B.

Step J4 is for producing compound (80) and implemented by reacting compound (137) with a metal alkoxide in an alcoholic solvent to make a reactive derivative of compound (137) and reacting it with compound (79) in an alcoholic solvent. The reaction is performed as in the aforementioned step B4 in process B.

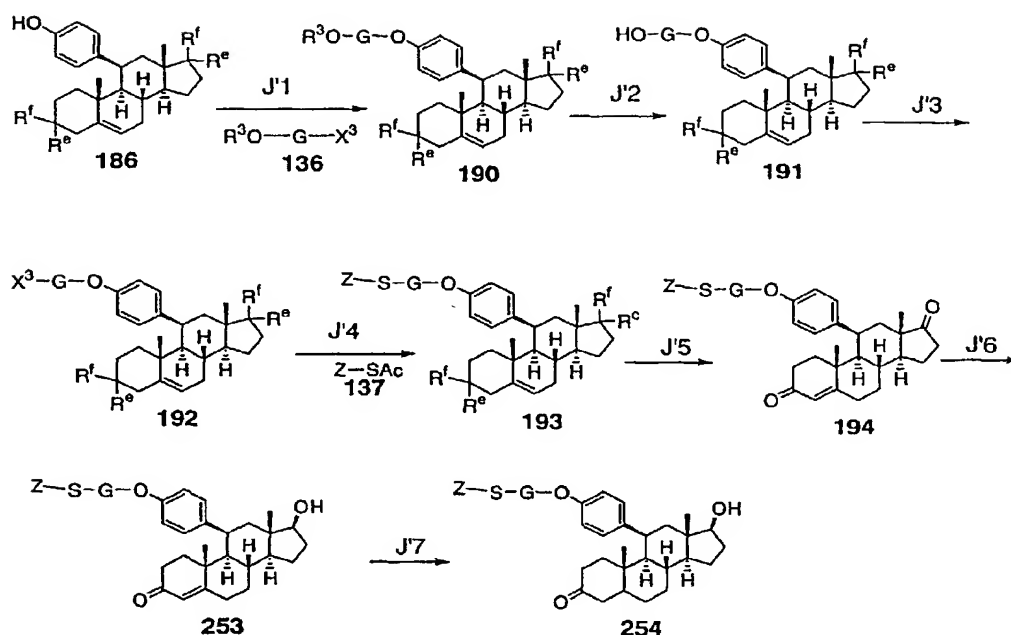
Step J5 is for producing compound (81) and implemented by reacting compound (80) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step A5 in process A.

Step J6 is for producing compound (82) and implemented by reacting compound (81) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A8 in process A.

Step J7 is for producing compound (83) and implemented by reacting compound (82) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step B7 in process B.

Process J' is an alternative method for producing compound (253) having the dashed line in compound (81) forming a double bond together with the solid line, and compound (254) having the dashed line in compound (81) forming a single bond together with the solid line.

25 Process J'



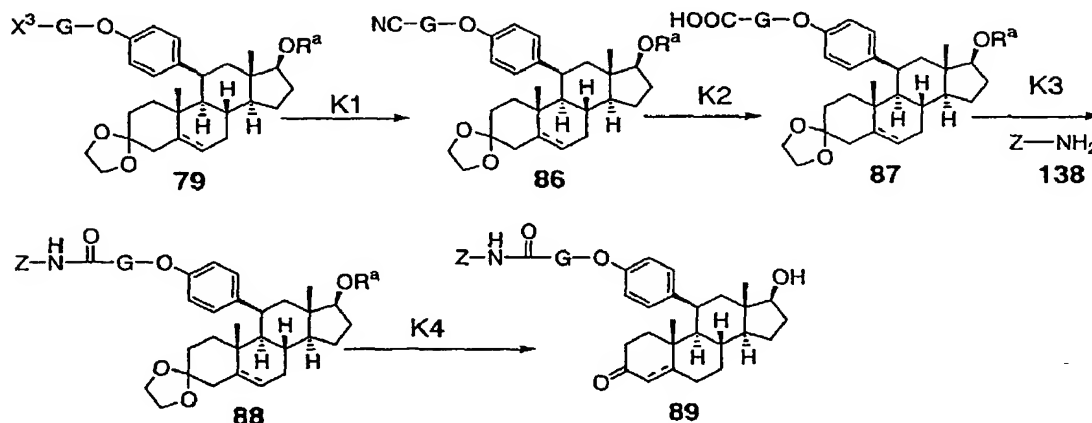
Step J'1 is for producing compound (190) and implemented by reacting compound (186) with a base in an inert solvent to make a salt of compound (186) and reacting it with compound (136) in an inert solvent. The reaction is performed as in the aforementioned step J1 in process J.

Step J'2 is for producing compound (191) and implemented by reacting compound (190) with a deprotecting agent, namely, removing the substituted silyl group, in an inert solvent. The reaction is performed as in the aforementioned step J2 in process J.

Step J'3 is for producing compound (192) and implemented by reacting compound (191) with a sulfonyl chloride compound in an amine-containing solvent or reacting compound (191) with a halogenating agent in an inert solvent. The reaction is performed as in the

R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond.

5 Process K



Step K1 is for producing compound (86) and implemented by reacting compound (79) with a cyanylating agent in an inert solvent. The reaction is performed as in the
10 aforementioned step C1 in process C.

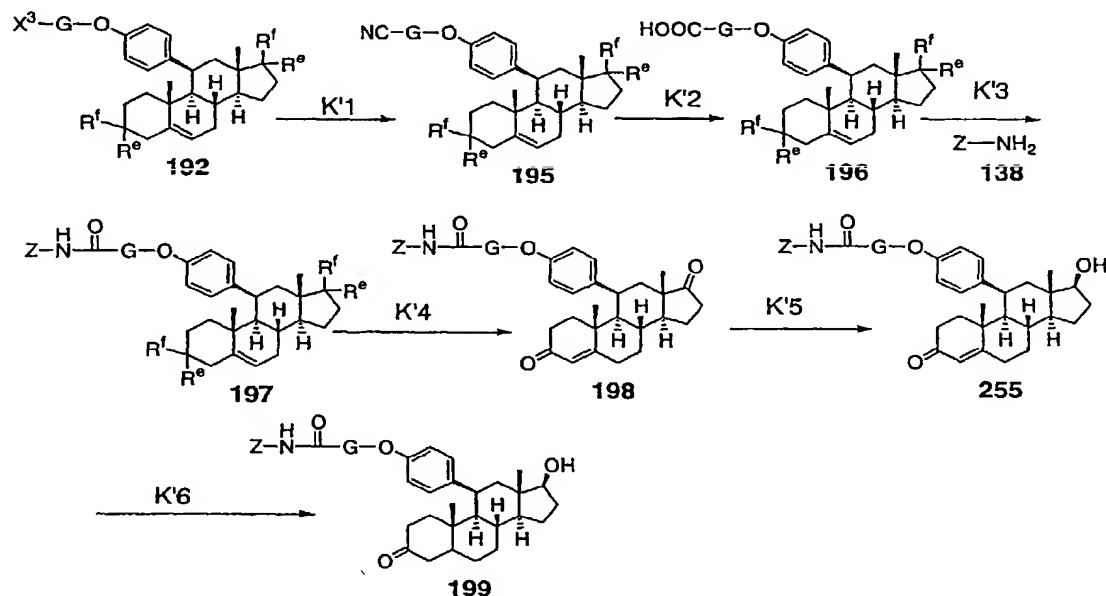
Step K2 is for producing compound (87) and implemented by hydrolyzing compound (86) in the presence of a base. The reaction is performed as in the aforementioned step C2 in process C.

15 Step K3 is for producing compound (88) and implemented by reacting compound (87) or reactive derivatives thereof (acid halides, mixed acid anhydrides or active esters) with compound (138) or acid addition salts thereof in an inert solvent. The reaction is performed as in the
20 aforementioned step C3 in process C.

Step K4 is for producing compound (89) and implemented by reacting compound (88) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step A5 in process A.

5 Process K' is an alternative method for producing compound (255) having the dashed line in compound (89) forming a double bond together with the solid line, and compound (199) having the dashed line in compound (89) forming a single bond together with the solid line.

10 Process K'



Step K'1 is for producing compound (195) and implemented by reacting compound (192) with a cyanylating agent in an inert solvent. The reaction is performed as in the aforementioned step K1 in process K.

Step K'2 is for producing compound (196) and implemented by hydrolyzing compound (195) in the presence

of a base. The reaction is performed as in the
aforementioned step K2 in process K.

Step K'3 is for producing compound (197) and
implemented by reacting compound (196) or reactive
5 derivatives thereof (acid halides, mixed acid anhydrides or
active esters) with compound (138) or acid addition salts
thereof in an inert solvent. The reaction is performed as
in the aforementioned step K3 in process K.

Step K'4 is for producing compound (198) and
10 implemented by reacting compound (197) with an acid in an
aqueous solvent. The reaction is performed as in the
aforementioned step J'5 in process J'.

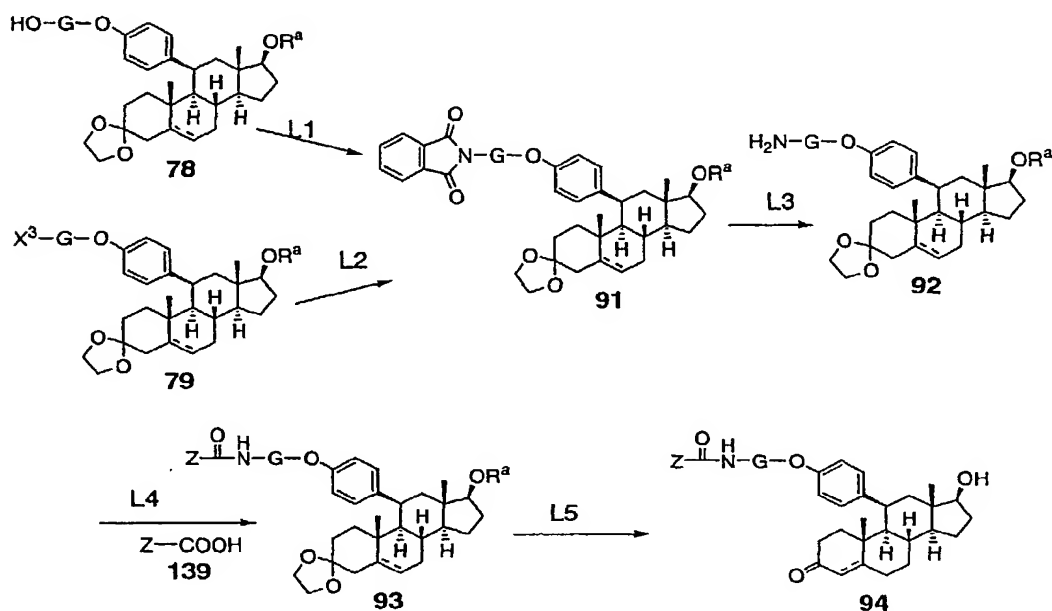
Step K'5 is for producing compound (255) and
implemented by reacting compound (198) with a reducing
15 agent in an optionally miscible inert solvent. The
reaction is performed as in the aforementioned step J'6 in
process J'.

Step K'6 is for producing compound (199) and
implemented by performing catalytic reduction of compound
20 (255) in an alcoholic solvent or an inert solvent or
reacting compound (255) with a reducing agent in an
optionally miscible inert solvent. The reaction is
performed as in the aforementioned step C'6 in process C'.

Process L is for producing compound (94) represented
25 by the general formula (I) in which X^1 is a group of β
configuration that is represented by the general formula
(II) in which Ar is an aromatic hydrocarbon group
(preferably a p-phenylene group), A is -O- and R^1 is -G-

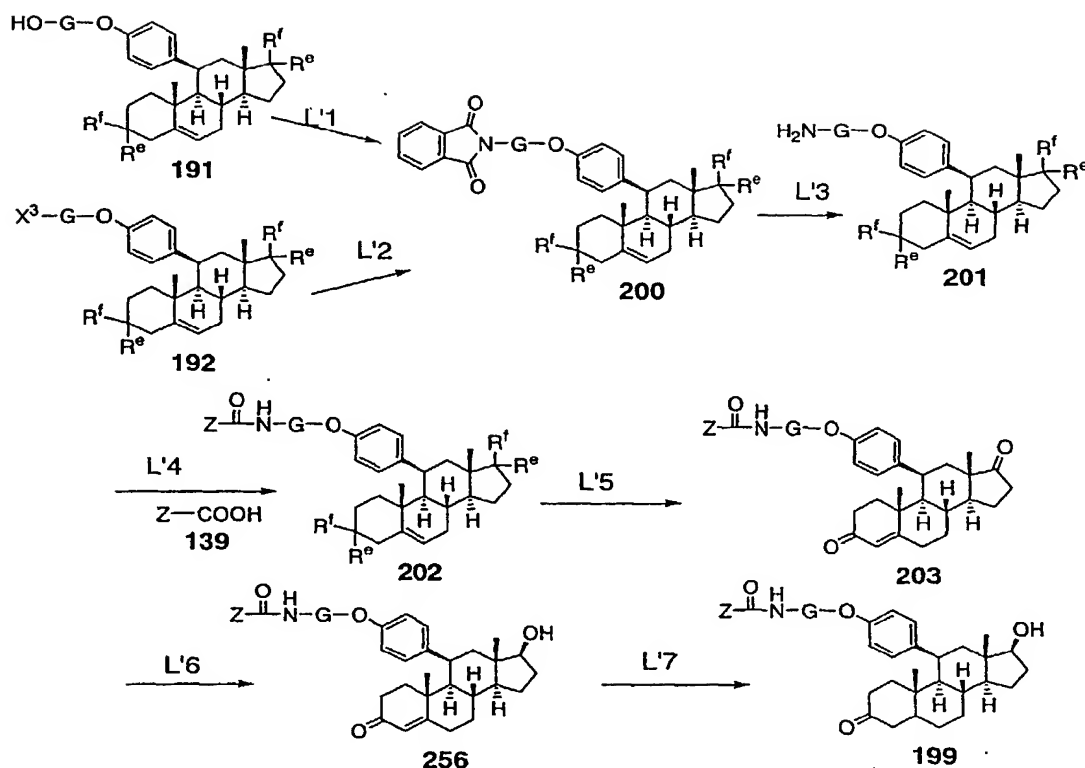
NHCO-Z, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond.

Process L



Step L1 is for producing compound (91) and implemented by reacting compound (78) with phthalimide in an inert solvent in the presence of an azodicarboxylic acid dialkyl ester (preferably diethyl azodicarboxylate) and a phosphine compound (preferably triphenylphosphine). The reaction is performed as in the aforementioned step D1 in process D.

Step L2 is an alternative step for producing compound (91) and implemented by reacting compound (79) with a metal salt of phthalimide (preferably phthalimide potassium) in an inert solvent. The reaction is performed as in the



Step L'1 is for producing compound (200) and implemented by reacting compound (191) with phthalimide in an inert solvent in the presence of an azodicarboxylic acid dialkyl ester (preferably diethyl azodicarboxylate) and a phosphine compound (preferably triphenylphosphine). The reaction is performed as in the aforementioned step L1 in process L.

Step L'2 is an alternative step for producing compound (200) and implemented by reacting compound (192) with a metal salt of phthalimide (preferably phthalimide potassium) in an inert solvent. The reaction is performed as in the aforementioned step L2 in process L.

Step L'3 is for producing compound (201) and

implemented by reacting compound (200) with an amine-containing compound (preferably hydrazine) in an alcoholic solvent. The reaction is performed as in the aforementioned step L3 in process L.

5 Step L'4 is for producing compound (202) and implemented by reacting compound (139) or reactive derivatives thereof (acid halides, mixed acid anhydrides or active esters) with compound (201) or acid addition salts thereof in an inert solvent. The reaction is performed as
10 in the aforementioned step L4 in process L.

 Step L'5 is for producing compound (203) and implemented by reacting compound (202) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step K'4 in process K'.

15 Step L'6 is for producing compound (256) and implemented by reacting compound (203) with a reducing agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step K'5 in
process K.

20 Step L'7 is for producing compound (199) and implemented by performing catalytic reduction of compound (256) in an alcoholic solvent or an inert solvent or by reacting compound (256) with a reducing agent in an optionally miscible inert solvent. The reaction is
25 performed as in the aforementioned step C'6 in process C'.

 Process M is for producing compound (102) represented by the general formula (I) in which X^1 is a hydrogen atom, X^2 is a group of α configuration that is represented by the

general formula (II) in which Ar is a single bond, A is -O- and R¹ is -(CH₂)₄- R², R^a is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond;

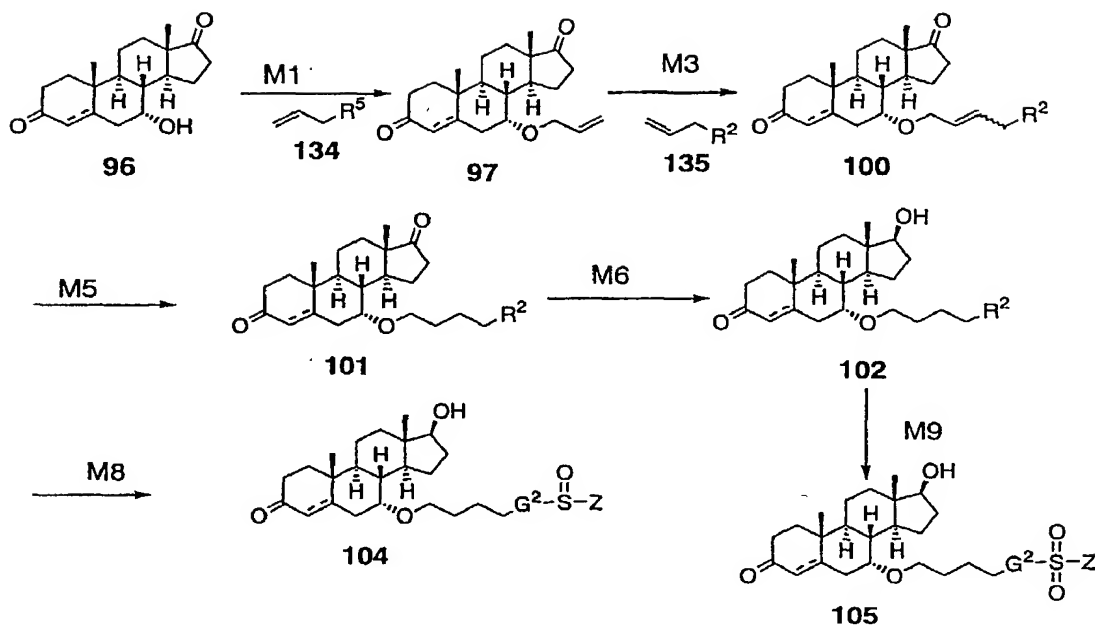
5 compound (104) represented by the general formula (I) in which X¹ is a hydrogen atom, X² is a group of α configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R¹ is

10 -(CH₂)₄-G²-S(O)-Z, R^a is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond; and

15 compound (105) represented by the general formula (I) in which X¹ is a hydrogen atom, X² is a group of α configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R¹ is

20 -(CH₂)₄-G²-S(O)₂-Z, R^a is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond.

Process M



Step M1 is for producing compound (97) and implemented by reacting compound (96) with a base in an inert solvent to make a salt of compound (96) and then reacting it with compound (134) in an inert solvent. The reaction is performed as in the aforementioned step A3 in process A.

A compound having the hydroxyl group in 7-position of compound (96) oriented in β configuration is also known by being disclosed in, for example, J. Org. Che., 26, 2856-2859 (1961) and by using this compound in place of compound (96), one can obtain compounds having X^2 in compound (102), compound (104) and compound (105) oriented in β configuration.

Step M3 is for producing compound (100) and implemented by reacting compound (97) with compound (135) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the

aforementioned step A4 in process A.

Step M5 is for producing compound (101) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step A6 in process A.

Step M6 is for producing compound (102) and implemented by reacting compound (101) with a reducing agent in an optionally miscible inert solvent.

The inert solvent to be used is not limited in any particular way as long as it does not interfere with the reaction; examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, alcoholic solvents such as methanol and ethanol, aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, and amines such as pyridine and triethylamine, and preferred examples are alcoholic solvents such as methanol and ethanol, with metanol being more preferred. The reducing agent to be used may be exemplified by: metal hydrogen complex compounds such as aluminum lithium hydride, trimethoxyaluminum lithium hydride, tri-t-butoxyaluminum lithium hydride, aluminum lithium hydride-trichloroaluminum (alane), aluminum lithium hydride-boron trifluoride, aluminum hydride magnesium chloride, magnesium aluminum hydride, sodium aluminum hydride, sodium triethoxyaluminum hydride, sodium bis(methoxyethoxy)aluminum hydride, sodium boron hydride, sodium boron hydride-palladium/carbon, sodium boron hydrogensulfide, sodium boron hydrogencyanide, sodium

trimethoxyboron hydride, lithium boron hydride, lithium boron hydrogencyanide, lithium triethylboron hydride, lithium tri-s-butylboron hydride, lithium tri-t-butylboron hydride, calcium boron hydride, potassium boron hydride, 5 potassium triisopropoxyboron hydride, potassium tri-s-butylboron hydride, zinc boron hydride, tetramethylammonium boron hydride, and tetra-n-butylammonium cyanoboron hydride; metal hydrides such as diisobutylaluminum hydride, triphenyltin hydride, tri-n-butyltin hydride, diphenyltin 10 hydride, di-n-butyltin hydride, triethyltin hydride, trimethyltin hydride, trichlorosilane/tri-n-butylamine, trichlorosilane/tri-n-propylamine, triethylsilane, trimethylsilane, diphenylsilane, phenylsilane, polymethylhydrosiloxane, dimethylphenylsilane, di-n- 15 butylsilane, and methylphenylsilane; borane derivatives such as diborane, dimethylamine-borane, trimethylamine-borane, ethylenediamine-borane, pyridine-borane, dimethylsulfide-borane, 2,3-dimethyl-2-butylborane (thexylborane), bis-3-methyl-2-butylborane (disiamylborane), 20 diisopinocanepherylborane, dicyclohexylborane, and 9-borabicyclo[3,3,1]nonane (9-BBN); preferred examples are metal hydrogen complex compounds such as aluminum lithium hydride, trimethoxyaluminum lithium hydride, tri-t-butoxyaluminum lithium hydride, aluminum lithium hydride- 25 trichloroaluminum (alane), aluminum lithium hydride-boron trifluoride, aluminum hydride magnesium chloride, magnesium aluminum hydride, sodium aluminum hydride, sodium triethoxyaluminum hydride, sodium

bis(methoxyethoxy)aluminum hydride, sodium boron hydride, sodium boron hydride-palladium/carbon, sodium boron hydrogensulfide, sodium boron hydrogencyanide, sodium trimethoxyboron hydride, lithium boron hydride, lithium boron hydrogencyanide, lithium triethylboron hydride, lithium tri-s-butylboron hydride, lithium tri-t-butylboron hydride, calcium boron hydride, potassium boron hydride, potassium triisopropoxyboron hydride, potassium tri-s-butylboron hydride, zinc boron hydride, tetramethylammonium boron hydride, and tetra-n-butylammonium cyanoboron hydride, with sodium boron hydride being more preferred. The reaction temperature which varies with the type of solvent and the like is typically in the range of -30°C ~ 100°C, preferably 0°C ~ 70°C. The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 48 hours, preferably 30 minutes - 24 hours.

Step M8 is for producing compound (104) in the case where Q² in R² in compound (102) is -S- and implemented by reacting compound (102) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A8 in process A.

Step M9 is for producing compound (105) in the case where Q² in R² in compound (102) is -S- and implemented by reacting compound (102) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A9 in process A.

Process N is for producing compound (112) represented

they are bound, are $-(C=O)$, and the dashed line together with the solid line is a double bond; compound (116) represented by the general formula (I) in which X^1 is a hydrogen atom and X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-(CH_2)_3-G^3-S(O)_2-Z$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a double bond; compound (117) represented by the general formula (I) in which X^1 is a hydrogen atom, X^2 is a group of α configuration represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-(CH_2)_3-G^3-S(O)-Z$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)$, and the dashed line together with the solid line is a single bond; and compound (118) represented by the general formula (I) in which X^1 is a hydrogen atom and X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-(CH_2)_3-G^3-S(O)_2-Z$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond.

Process N

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ethylene glycol, 1,3-propanediol, 1,4-butanediol, and 1,5-pentanediol, ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, 5 halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, as well as cyclohexane, dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone, dimethylformamide, N-methylpyrrolidone, ethyl acetate, acetonitrile and 10 nitromethane; preferred examples are methanol and ethanol.

The condition to be used in catalytic reduction is a homogeneous system such as hydrogen-chlorotris(triphenylphosphine)rhodium(I), hydrogen-chlorotris(triparatolylphosphine)rhodium(I), hydrogen-15 chlorotris(triparamethoxyphenylphosphine)rhodium(I), hydrogen-hydridecarbonyltris(triphenylphosphine)rhodium(I), hydrogen-rhodium(II) acetate, hydrogen-ruthenium(II) acetate, hydrogen-chlorohydridetris(triphenylphosphine)ruthenium(II), 20 hydrogen-carboxylatohydridetris(triphenylphosphine)ruthenium(II), hydrogen-hydridecarbonyltris(triphenylphosphine)iridium(I), hydrogen-platinum(II)-tin chloride complex, hydrogen-pentacyanocobalt(II) complex, hydrogen-tricyanobipyridine 25 cobalt(II) complex, hydrogen-bis(dimethylglyoximato)cobalt(II) complex, hydrogen-methyl benzoate-tricarbonylchromium complex, hydrogen-bis(tricarbonylcyclopentadienylchromium), hydrogen-

pentacarbonyliron, hydrogen-
 bis(cyclopentadienyl)dicarbonyltitanium, hydrogen-
 hydridecarbonylcobalt complex, hydrogen-
 octacarbonyldicobalt, hydrogen-hydridecarbonylrhodium,
 5 hydrogen-chromium(III) acetylacetonato-triisobutylaluminum,
 hydrogen-cobalt(II) acetylacetonato-triisobutylaluminum, or
 hydrogen-nickel(II)-2-hexanoato-triethylaluminum, or an
 inhomogeneous system condition such as hydrogen-platinum
 dioxide, hydrogen-platinum/carbon, hydrogen-
 10 palladium/carbon, hydrogen-palladium/barium sulfate,
 hydrogen-palladium/calcium carbonate, hydrogen-Raney nickel,
 hydrogen-copper chromite, hydrogen-rhodium/carbon,
 hydrogen-rhodium/alumina, hydrogen-ruthenium dioxide, or
 hydrogen-ruthenium/carbon; a preferred example is hydrogen-
 15 palladium/carbon.

The reaction temperature is typically in the range of
 0°C - 100°C, preferably 0°C - 60°C. The reaction time which
 varies with the reaction temperature and the like is
 typically in the range of 10 minutes - 24 hours, preferably
 20 10 minutes - 6 hours.

Step N7 is for producing compound (115) in the case
 where Q^4 in R^2 in compound (113) is -S- and implemented by
 reacting compound (113) with an oxidizing agent in an inert
 solvent. The reaction is performed as in the
 25 aforementioned step A8 in process A.

Step N8 is for producing compound (116) in the case
 where Q^4 in R^2 in compound (113) is -S- and implemented by
 reacting compound (113) with an oxidizing agent in an inert

solvent. The reaction is performed as in the
aforementioned step A9 in process A.

Step N9 is for producing compound (117) in the case
where Q^4 in R^2 in compound (114) is -S- and implemented by
5 reacting compound (114) with an oxidizing agent in an inert
solvent. The reaction is performed as in the
aforementioned step A8 in process A.

Step N10 is for producing compound (118) in the case
where Q^4 in R^2 in compound (114) is -S- and implemented by
10 reacting compound (114) with an oxidizing agent in an inert
solvent. The reaction is performed as in the
aforementioned step A9 in process A.

Step N11 is an alternative method of producing
compound (114) and implemented by performing catalytic
15 reduction in an alcoholic solvent or an inert solvent. The
reaction is performed as in the aforementioned step N6 in
process N.

Process O is for producing compound (126) represented
by the general formula (I) in which X^1 is a hydrogen atom,
20 X^2 is a group of α configuration that is represented by the
general formula (II) in which Ar is an aromatic hydrocarbon
group (preferably a p-phenylene group), A is -O- and R^1 is
-CH₂-CH=CH-CH₂-R², R^a is a hydrogen atom, R^b and R^c, when
taken together with the carbon atom in 3-position to which
25 they are bound, are -(C=O)-, and the dashed line together
with the solid line is a double bond; compound (127)
represented by the general formula (I) in which X^1 is a
hydrogen atom, X^2 is a group of α configuration that is



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limited in any particular way and may be exemplified by fluorides such as hydrogen fluoride, hydrogen fluoride-pyridine, sodium fluoride, potassium fluoride and tetra-n-butylammonium fluoride, inorganic acids such as

- 5 hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid and phosphoric acid, and organic acids such as formic acid, acetic acid and p-toluenesulfonic acid, with tetra-n-butylammonium fluoride being preferred.

The reaction temperature which varies with the type of
10 solvent and the like is typically in the range of 0°C - 80°C (preferably 0°C - 50°C). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 15 hours).

- 15 Step 03 is for producing compound (122) and implemented by reacting compound (121) with a base in an inert solvent to make a salt of compound (121) and then reacting it with compound (134) in an inert solvent. The reaction is performed as in the aforementioned step A3 in
20 process A.

- Step 05 is for producing compound (125) and implemented by reacting compound (122) with compound (135) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the
25 aforementioned step A4 in process A.

Step 06 is for producing compound (126) and implemented by hydrolyzing compound (125) in water or a water-soluble solvent in the presence of a base or an acid

performed as in the aforementioned step A6 in process A.

Step O9 is for producing compound (128) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step N6 in process N.

Step O10 is for producing compound (129) in the case where Q^2 in R^2 in compound (127) is -S- and implemented by reacting compound (127) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A8 in process A.

Step O11 is for producing compound (130) in the case where Q^2 in R^2 in compound (127) is -S- and implemented by reacting compound (127) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A9 in process A.

Step O12 is for producing compound (131) in the case where Q^2 in R^2 in compound (128) is -S- and implemented by reacting compound (128) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A8 in process A.

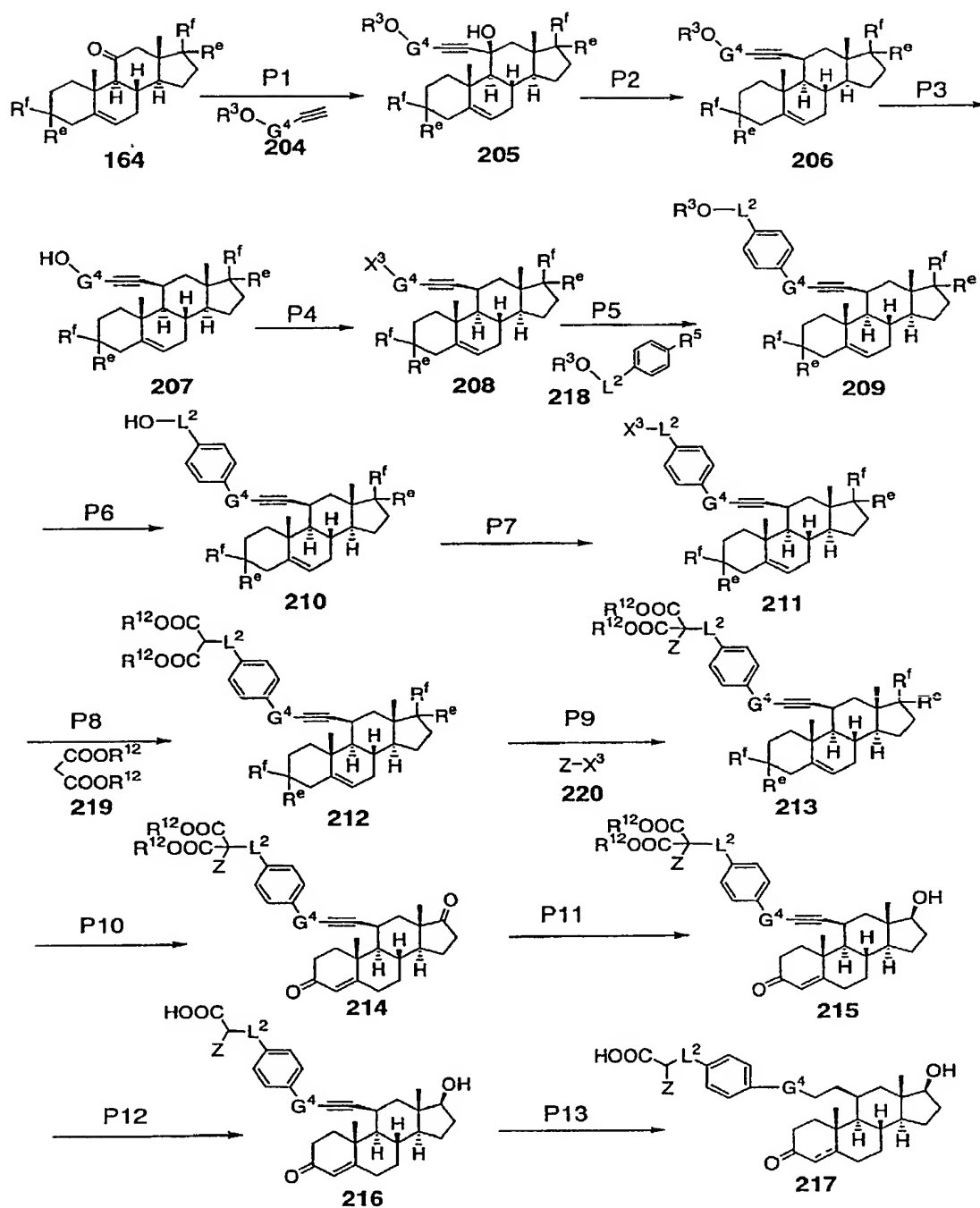
Step O13 is for producing compound (132) in the case where Q^2 in R^2 in compound (128) is -S- and implemented by reacting compound (128) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A9 in process A.

Process P is for producing compound (217) represented by the general formula (I) in which X^2 is a hydrogen atom, X^1 is a group of β configuration that is represented by the

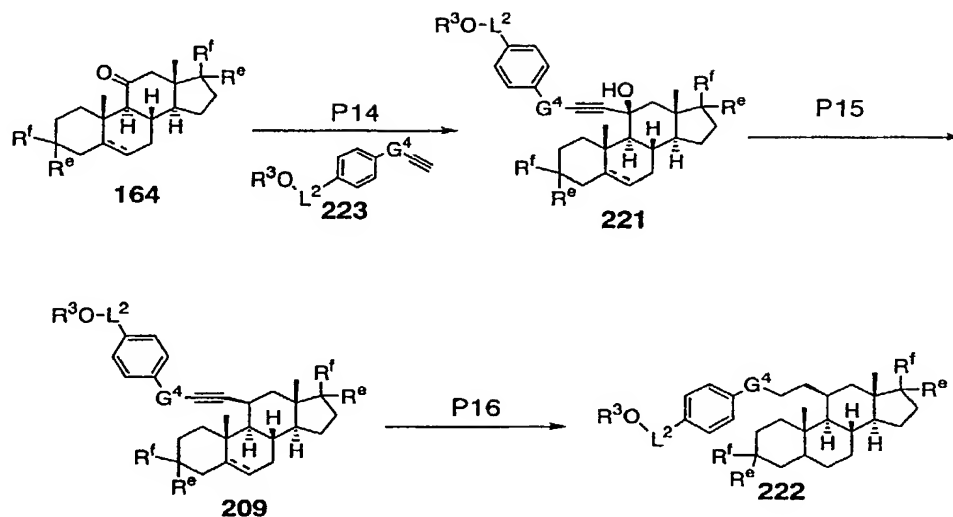
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general formula (II) in which Ar is single bond, A is a methylene group and R^1 is a group represented by the general formula (III) in which G is $-G^4-CH_2-$, E is a single bond, J is an optionally substituted aromatic hydrocarbon group (preferably a p-phenylene group), Y is a single bond, L is L^2 , Q is Q^{17} , with R^7 in Q^{17} being a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond.

Process P



Process P (continued)



Step P1 is for producing compound (205) and implemented by reacting compound (204) with an alkyllithium (preferably n-butyllithium) in an inert solvent to make a reactive derivative of compound (204) and reacting it with compound (164) in an inert solvent. The reaction is performed as in the aforementioned step F1 in process F.

Step P2 is for producing compound (206) and implemented by reacting compound (205) with a reducing agent in an inert solvent in the presence of an additive. The reaction is performed as in the aforementioned step F2 in process F.

In this step, a compound having the substituent in the 11-position of compound (206) oriented in α configuration forms as a by-product and this may be used to give a compound having X^1 in compound (217) oriented in α configuration.

Step P3 is for producing compound (207) and implemented by reacting compound (206) with a deprotecting agent, namely, removing the substituted silyl group, in an inert solvent. The reaction is performed as in the
5 aforementioned step F3 in process F.

Step P4 is for producing compound (208) and implemented by reacting compound (207) with a sulfonyl chloride compound in an amine-containing solvent or reacting compound (207) with a halogenating agent in an
10 inert solvent. The reaction is performed as in the aforementioned step F4 in process F.

Step P5 is for producing compound (209) and implemented by reacting compound (218) with a metal (preferably magnesium) or an alkyllithium (preferably n-
15 butyllithium) in an inert solvent to make a reactive derivative of compound (218) and reacting it with compound (208) in an inert solvent. The reaction is performed as in the aforementioned step I1 in process I.

Step P6 is for producing compound (210) and
20 implemented by reacting compound (209) with a deprotecting agent, namely, removing the substituted silyl group, in an inert solvent. The reaction is performed as in the aforementioned step P3 in process P.

Step P7 is for producing compound (211) and
25 implemented by reacting compound (210) with a sulfonyl chloride compound in an amine-containing solvent or reacting compound (210) with a halogenating agent in an inert solvent. The reaction is performed as in the

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aforementioned stepp P4 in process P.

Step P8 is for producing compound (212) and implemented by reacting compound (219) with a base in an inert solvent to make a reactive derivative of compound (219) and then reacting it with compound (211) in an inert solvent.

The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction; examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, as well as dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone, dimethylformamide, and N-methylpyrrolidone; preferred examples are ether solvents such as tetrahydrofuran, as well as dimethylformamide. The base to be used may be exemplified by metal alkoxides such as sodium alkoxide and potassium t-butoxide, metal hydrides such as sodium hydride, potassium hydride and calcium hydride, alkyl lithium compounds such as methyl lithium, ethyl lithium, n-butyl lithium and t-butyl lithium, metal amides such as sodium amide, potassium bistrimethylsilylamide, sodium bistrimethylsilylamide and lithium diisopropylamide, as well as carbonates such as cesium carbonate, potassium carbonate and sodium carbonate; preferred examples are metal hydrides such as sodium hydride, metal amides such as lithium diisopropylamide, and carbonates such as cesium carbonate.

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The reaction temperature which varies with the type of solvent and the like is typically in the range of -78°C ~ 80°C , preferably 0°C ~ 30°C . The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 24 hours, preferably 30 minutes - 15 hours.

Step P9 is for producing compound (213) and implemented by reacting compound (212) with a base in an inert solvent to make a reactive derivative of compound (212) and then reacting it with compound (220) in an inert solvent. The reaction is performed as in the aforementioned step P8 in process P.

If Z is a hydrogen atom in process P, step P9 may be omitted.

Step P10 is for producing compound (214) and implemented by reacting compound (213) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step L'5 in process L'.

Step P11 is for producing compound (215) and implemented by reacting compound (214) with a reducing agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step L'6 in process L'.

Step P12 is for producing compound (216) and implemented by reacting compound (215) with an acid, a base or a metal salt in an hydrous alcohol or an inert solvent.

The solvents to be used are not limited in any particular way as long as they do not interfere with the

reaction; examples are mixtures of water and alcoholic solvents such as methanol, ethanol, n-propanol, i-propanol, n-butanol, s-butanol and t-butanol, amine-containing solvents such as pyridine, as well as dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone and dimethylformamide; preferred examples are a mixture of water and an alcoholic solvent such as methanol or ethanol, and dimethyl sulfoxide.

The acid to be used may be exemplified by inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid and phosphoric acid, with hydrochloric acid and hydrobromic acid being preferred.

The base to be used may be exemplified by metal hydroxides such as lithium hydroxide, sodium hydroxide, potassium hydroxide, potassium hydroxide, calcium hydroxide, barium hydroxide and cesium hydroxide, with sodium hydroxide and potassium hydroxide being preferred.

The metal salt to be used can be lithium chloride, sodium cyanide, etc., with lithium chloride being preferred.

The reaction temperature which varies with the type of solvent and the like is typically in the range of 25°C - 180°C, preferably 40°C - 150°C. The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 24 hours, preferably 30 minutes - 15 hours.

Step P13 is for producing compound (217) and implemented by performing catalytic reduction of compound (216) in an alcoholic solvent or an inert solvent. The

reaction is performed as in the aforementioned step F8 in process F.

As an ancillary to this reaction, conversion to a single bond may occasionally be effected if the dashed line
5 forms a double bond together with the solid line.

Steps P14 and P15 provide an alternative method of producing compound (209).

Step P14 is for producing compound (221) and implemented by reacting compound (223) with an alkyllithium
10 (preferably n-butyllithium) in an inert solvent to make a reactive derivative of compound (223) and reacting it with compound (164) in an inert solvent. The reaction is performed as in the aforementioned step P1 in process P.

Step P15 is for producing compound (209) and
15 implemented by reacting compound (209) with a reducing agent in an inert solvent in the presence of an additive. The reaction is performed as in the aforementioned step P2 in process P.

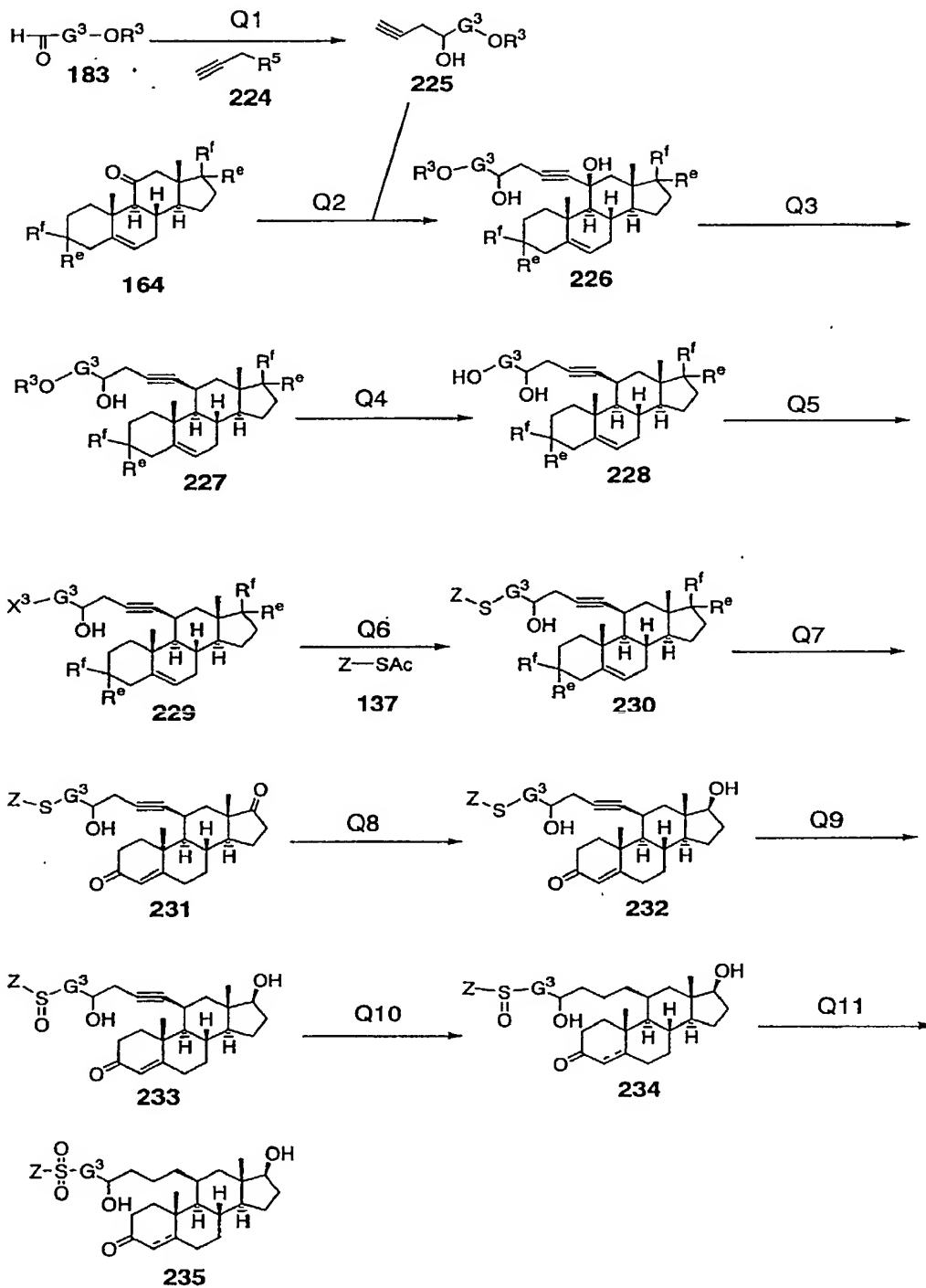
In this step, a compound having the substituent in the
20 11-position of compound (209) oriented in α configuration forms as a by-product and this may be used to give a compound having X^1 in compound (217) oriented in α configuration.

Step P16 is for producing compound (222) and
25 implemented by performing catalytic reduction of compound (209) in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step P13 in process P.

By subjecting compound (222) to step P6 as in the case of compound (209), one can produce a compound having the dashed line in compound (217) forming a single bond together with the solid line.

5 Process Q is for producing compound (234) represented by the general formula (I) in which X^2 is a hydrogen atom, X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is single bond, A is a methylene group and R^1 is a group represented by the
 10 general formula (III) in which G is $-(CH_2)_2-CH(OH)-G^3-$, E, J, Y and L are single bonds, and Q is Q^{63} , R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond
 15 or a double bond; and compound (235) represented by the general formula (I) in which X^2 is a hydrogen atom, X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is single bond, A is a methylene group and R^1 is a group represented by the general formula
 20 (III) in which G is $-(CH_2)_2-CH(OH)-G^3-$, E, J, Y and L are single bonds, and Q is Q^{64} , R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double
 25 bond.

Process Q



Step Q1 is for producing compound (225) and
 implemented by reacting compound (224) with a metal

(preferably magnesium) or an alkyllithium (preferably t-butylolithium) in an inert solvent in the presence or absence (preferably the presence) of an additive {preferably mercury(II) chloride} to make a reactive derivative of compound (224) and reacting it with compound (183) in an inert solvent.

The inert solvent to be used is not limited in any particular way as long as it does not participate in the reaction; preferred examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, with ether and tetrahydrofuran being more preferred.

The reaction temperature which varies with the type of solvent and the like is typically in the range of 0°C - 80°C (preferably 10°C - 50°C). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 15 hours).

Step Q2 is for producing compound (226) and implemented by reacting compound (225) with an alkyllithium (preferably n-butylolithium) in an inert solvent to make a reactive derivative of compound (225) and reacting it with compound (164) in an inert solvent. The reaction is performed as in the aforementioned step F1 in process F.

Step Q3 is for producing compound (227) and implemented by reacting compound (226) with a reducing agent in an inert solvent in the presence of an additive. The reaction is performed as in the aforementioned step F2 in process F.

agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step P11 in process P.

Step Q9 is for producing compound (233) and
5 implemented by reacting compound (232) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step F6 in process F.

Step Q10 is for producing compound (234) and
implemented by performing catalytic reduction of compound
10 (233) in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step F8 in process F.

As an ancillary to this reaction, conversion to a single bond may occasionally be effected if the dashed line
15 forms a double bond together with the solid line.

Step Q11 is for producing compound (235) and implemented by reacting compound (234) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step B7 in process B.

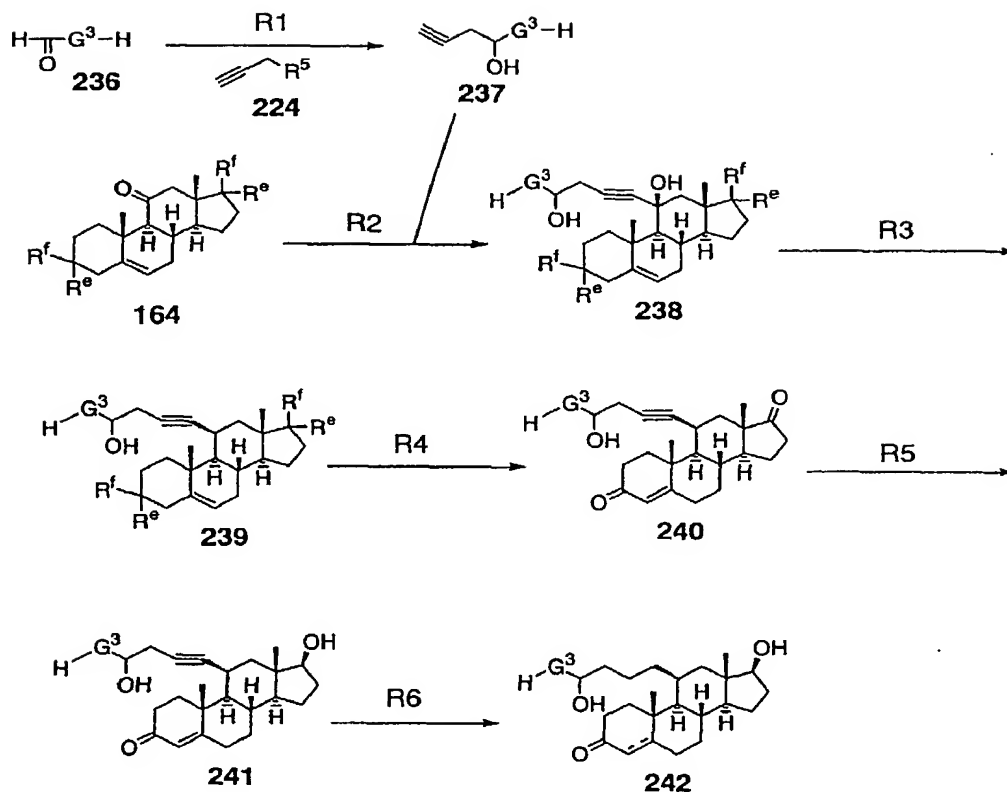
20 In process Q, step Q5, step Q6, step Q9 and step Q11 may be omitted and by so doing, one can produce a compound represented by the general formula (I) in which X^2 is a hydrogen atom, X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is
25 single bond, A is a methylene group and R^1 is a group represented by the general formula (III) in which G is $-(CH_2)_2-CH(OH)-G^3-$, E, J, Y, L and Q are single bonds, and Z is $-O-R^d$, R^a is a hydrogen atom, R^b and R^c , when taken

together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond.

In process Q, the hydroxyl group on G may optionally
5 be subjected to a protecting reaction and a deprotecting reaction in any desired steps.

Process R is a method for producing compound (242) represented by the general formula (I) in which X^2 is a hydrogen atom, X^1 is a group of β configuration that is
10 represented by the general formula (II) in which Ar is single bond, A is a methylene group and R^1 is a group represented by the general formula (III) in which G is $-(CH_2)_2-CH(OH)-G^3-$, E, J, Y, L and Q are single bonds, and Z is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when
15 taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond.

Process R



Step R1 is for producing compound (237) and implemented by reacting compound (224) with a metal (preferably magnesium) or an alkyllithium (preferably t-butylolithium) in an inert solvent in the presence or absence (preferably the presence) of an additive {preferably mercury(II) chloride} to make a reactive derivative of compound (224) and reacting it with compound (236) in an inert solvent. The reaction is performed as in the aforementioned step Q1 in process Q.

Step R2 is for producing compound (238) and implemented by reacting compound (237) with an alkyllithium (preferably n-butylolithium) in an inert solvent to make a reactive derivative of compound (237) and reacting it with

compound (164) in an inert solvent. The reaction is performed as in the aforementioned step Q2 in process Q.

Step R3 is for producing compound (239) and implemented by reacting compound (238) with a reducing agent in an inert solvent in the presence of an additive. The reaction is performed as in the aforementioned step Q3 in process Q.

As a by-product of this step, there is formed a compound having the substituent in 11-position of compound (239) oriented in α configuration; by using this compound, one can obtain a compound having X^1 in compound (242) oriented in α configuration.

Step R4 is for producing compound (240) and implemented by reacting compound (239) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step Q7 in process Q.

Step R5 is for producing compound (241) and implemented by reacting compound (240) with a reducing agent in an optionally miscible inert solvent. The reaction is performed as in the aforementioned step Q8 in process Q.

Step R6 is for producing compound (242) and implemented by performing catalytic reduction of compound (241) in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step Q10 in process Q.

As an ancillary to this reaction, conversion to a single bond may occasionally be effected if the dashed line

forms a double bond together with the solid line.

In process R, the hydroxyl group on G may optionally be subjected to a protecting reaction and a deprotecting reaction in any desired steps.

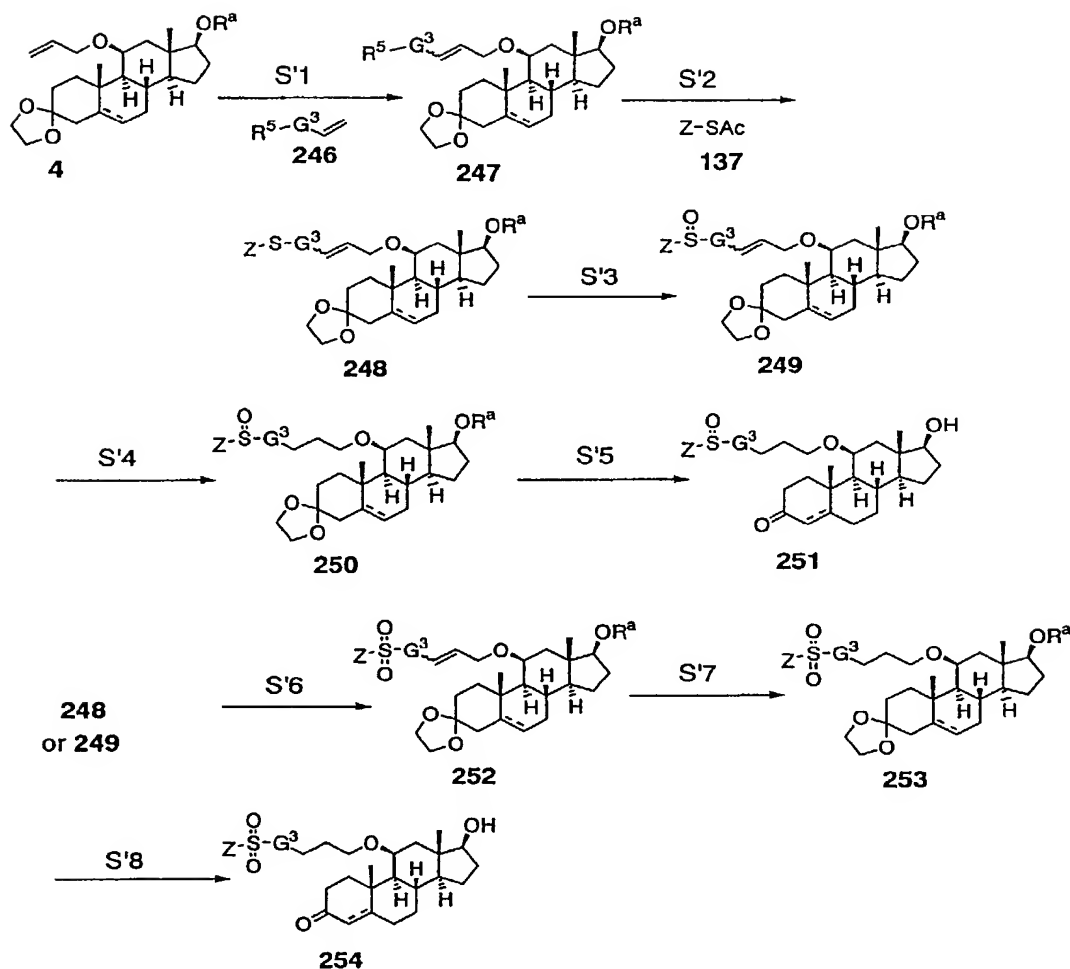
5 Process S is for producing compound (244) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{COOH}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond or a double bond; and compound (245) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{CON}(\text{R}^7)\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond or a double bond.

Process S

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by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R^1 is $-\text{CH}_2-\text{CH}_2-\text{G}^3-\text{SO}-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, 5 R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond or a double bond; and compound (254) represented by the general formula (I) in which X^1 is a group of β , 10 configuration that is represented by the general formula (II) in which Ar is a single bond, A is -O- and R^1 is $-\text{CH}_2-\text{CH}_2-\text{G}^3-\text{SO}_2-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the 15 dashed line together with the solid line is a single bond or a double bond.

Process S'



Step S'1 is for producing compound (247) and implemented by reacting compound (4) with compound (246) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the aforementioned step A4 in process A.

Step S'2 is for producing compound (248) and implemented by reacting compound (137) with a metal alkoxide in an alcoholic solvent to make a reactive derivative of compound (137) and reacting it with compound (247) in an alcoholic solvent. The reaction is performed

as in the aforementioned step B4 in process B.

Step S'3 is for producing compound (249) and implemented by reacting compound (248) with an oxidizing agent in an inert solvent. The reaction is performed as in
5 the aforementioned step A8 in process A.

Step S'4 is for producing compound (250) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step A6 in process A.

10 Step S'5 is for producing compound (251) and implemented by reacting compound (250) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step A5 in process A.

Step S'6 is for producing compound (252) and
15 implemented by reacting compound (248) or compound (249) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A9 in process A.

Step S'7 is for producing compound (253) and implemented by performing catalytic reduction in an
20 alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step A6 in process A.

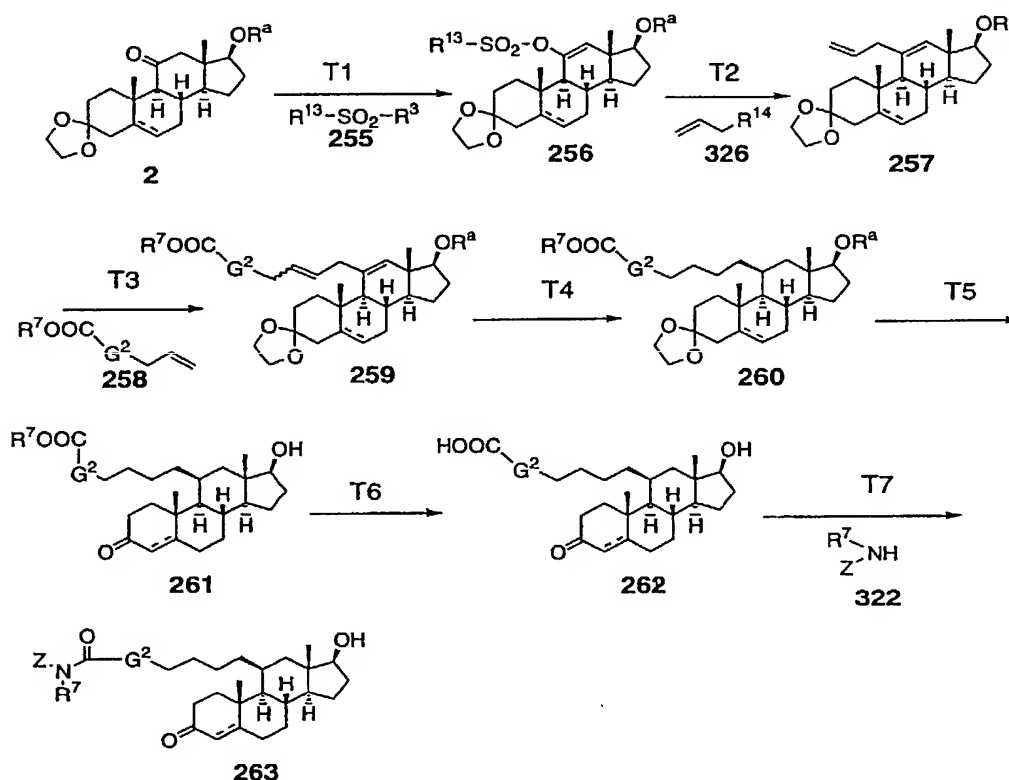
This step can also be implemented by using compound (250) as the starting material.

Step S'8 is for producing compound (254) and
25 implemented by reacting compound (253) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step A5 in process A.

This step can also be implemented by using compound

formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{CON}(\text{R}^7)-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond or a double bond.

Process T



Step T1 is for producing compound (256) and implemented by reacting compound (2) with a base in an inert solvent to make a reactive derivative of compound (2) and reacting it with compound (255) in an inert solvent.

The inert solvent to be used is not limited in any particular way as long as it does not participate in the

reaction; preferred examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, with tetrahydrofuran being more preferred. Preferred examples of the base to be used are n-butyllithium and lithium
 5 diisopropylamide. The reaction temperature which varies with the type of solvent and the like is typically in the range of $-100^{\circ}\text{C} \sim 50^{\circ}\text{C}$, preferably $-78^{\circ}\text{C} \sim 30^{\circ}\text{C}$. The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 48
 10 hours, preferably 30 minutes - 24 hours.

Step T2 is for producing compound (257) and implemented by reacting compound (256) with compound (326) in an inert solvent in the presence of a metal catalyst.

The inert solvent to be used is not limited in any
 15 particular way as long as it does not participate in the reaction; preferred examples are ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, with tetrahydrofuran being more preferred. The metal catalyst to be used is not limited in any particular way and may be
 20 exemplified by tetrakis(triphenylphosphine)palladium, palladium(II) acetate-triphenylphosphine, bis(triphenylphosphine)palladium(II) chloride, etc, with tetrakis(triphenylphosphine)palladium being preferred. The reaction temperature which varies with the type of solvent
 25 and the like is typically in the range of $0^{\circ}\text{C} - 100^{\circ}\text{C}$, preferably $10^{\circ}\text{C} - 80^{\circ}\text{C}$. The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 48 hours, preferably 30 minutes - 24

hours.

Step T3 is for producing compound (259) and implemented by reacting compound (257) with compound (258) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the
5
aforementioned step A4 in process A.

Step T4 is for producing compound (260) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent.

The solvent to be used may be exemplified by alcoholic solvents such as methanol, ethanol, n-propanol, i-propanol, n-butanol, s-butanol, t-butanol, pentanol, hexanol, cyclopropanol, cyclobutanol, cyclopentanol, cyclohexanol, ethylene glycol, 1,3-propanediol, 1,4-butanediol and 1,5-pentenediol, ether solvents such as ether, tetrahydrofuran, dioxane and dimethoxyethane, aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, as well as cyclohexane, dimethyl sulfoxide, dimethylacetamide, dimethylimidazolidinone, dimethylformamide, N-methylpyrrolidone, ethyl acetate, acetonitrile and nitromethane; preferred examples are ethanol, dioxane, benzene and ethyl acetate.

25 The condition to be used in catalytic reduction is a
homogeneous system such as hydrogen-
chlorotris(triphenylphosphine)rhodium(I), hydrogen-
chlorotris(triparatolylphosphine)rhodium(I), hydrogen-

chlorotris(triparamethoxyphenylphosphine)rhodium(I),
hydrogen-hydridecarbonyltris(triphenylphosphine)rhodium(I),
hydrogen-rhodium(II) acetate, hydrogen-ruthenium(II)
acetate, hydrogen-

5 chlorohydridetris(triphenylphosphine)ruthenium(II),
hydrogen-
carboxylatohydridetris(triphenylphosphine)ruthenium(II),
hydrogen-hydridecarbonyltris(triphenylphosphine)iridium(I),
hydrogen-platinum(II)-tin chloride complex, hydrogen-

10 pentacyanocobalt(II) complex, hydrogen-tricyanobipyridine
cobalt(II) complex, hydrogen-
bis(dimethylglyoximato)cobalt(II) complex, hydrogen-methyl
benzoate-tricarbonylchromium complex, hydrogen-
bis(tricarbonylcyclopentadienylchromium), hydrogen-

15 pentacarbonyliron, hydrogen-
bis(cyclopentadienyl)dicarbonyltitanium, hydrogen-
hydridecarbonylcobalt complex, hydrogen-
octacarbonyldicobalt, hydrogen-hydridecarbonylrhodium,
hydrogen-chromium(III) acetylacetonato-triisobutylaluminum,

20 hydrogen-cobalt(II) acetylacetonato-triisobutylaluminum, or
hydrogen-nickel(II)-2-hexanoato-triethylaluminum, or an
inhomogeneous system condition such as hydrogen-platinum
dioxide, hydrogen-platinum/carbon, hydrogen-
palladium/carbon, hydrogen-palladium hydroxide/carbon,

25 hydrogen-palladium/barium sulfate, hydrogen-
palladium/calcium carbonate, hydrogen-Raney nickel,
hydrogen-copper chromite, hydrogen-rhodium/carbon,
hydrogen-rhodium/alumina, hydrogen-ruthenium dioxide,

hydrogen-ruthenium/carbon, or hydrogen-iridium black; a preferred example is hydrogen-iridium black.

5 The reaction temperature is typically in the range of 0°C - 100°C, preferably 0°C - 60°C. The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 100 hours, preferably 10 hours - 96 hours.

Step T5 is for producing compound (261) and implemented by reacting compound (260) with an acid in an aqueous solvent. The reaction is performed as in the
10 aforementioned step A5 in process A.

In step T5, ester hydrolysis may occur and in that case, subsequent step T6 may be omitted.

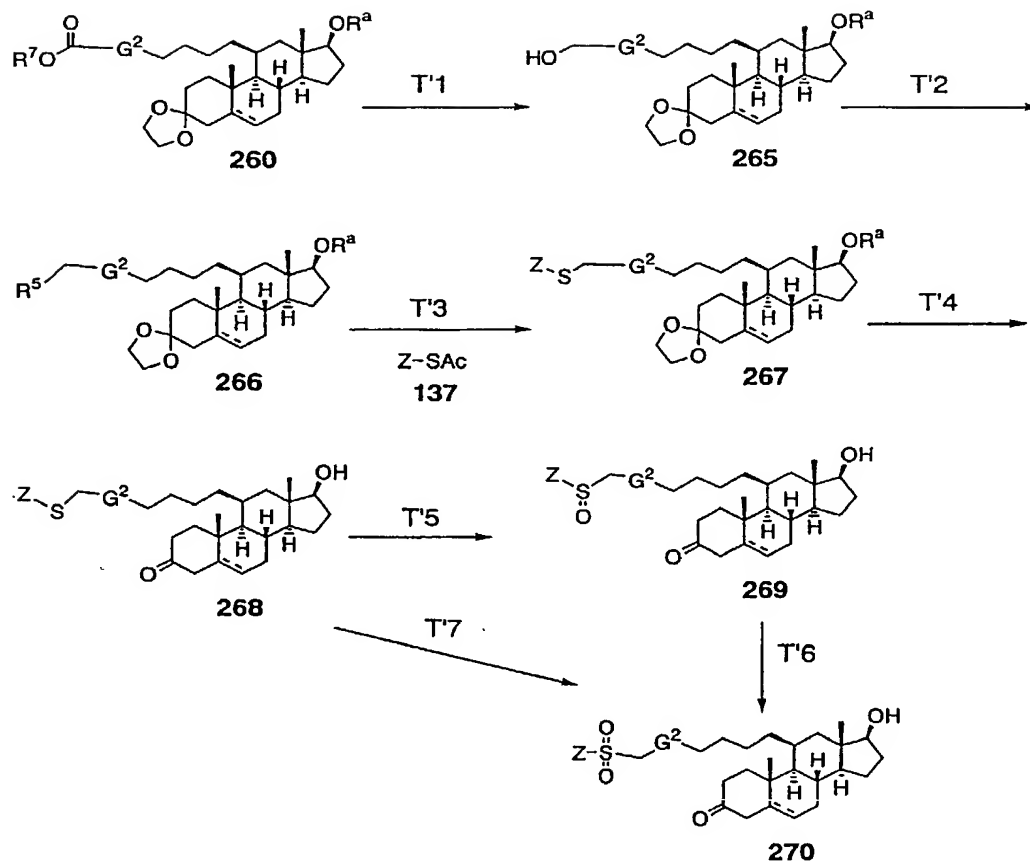
Step T6 is for producing compound (262) and
15 implemented by hydrolyzing compound (261) in water or a water-soluble solvent in the presence of a base or an acid (preferably a base). The reaction is performed as in the aforementioned step O6 in process O.

Step T7 is for producing compound (263) and
20 implemented by reacting compound (262) or reactive derivatives thereof (acid halides, mixed acid anhydrides or active esters) with compound (322) or acid addition salts thereof in an inert solvent. The reaction is performed as in the aforementioned step C3 in process C.

25 Process T' is for producing compound (268) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group

and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{CH}_2-\text{S}-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is
5 a single bond or a double bond; compound (269) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{CH}_2-\text{SO}-\text{Z}$, X^2 is a hydrogen atom, R^a
10 is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond or a double bond; and compound (270) represented by the general formula (I) in which X^1 is a
15 group of β configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{CH}_2-\text{SO}_2-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound,
20 are $-(\text{C}=\text{O})$, and the dashed line together with the solid line is a single bond or a double bond.

Process T'



Step T'1 is for producing compound (265) and implemented by reacting compound (260) with a reducing agent in an inert solvent and the reaction is performed as in the aforementioned step A2 in process A.

Step T'2 is for producing compound (266) and implemented by reacting compound (265) with a sulfonyl chloride compound in an amine-containing solvent or reacting compound (265) with a halogenating agent in an inert solvent. The reaction is performed as in the aforementioned step B3 in process B.

Step T'3 is for producing compound (267) and implemented by reacting compound (137) with a metal

alkoxide in an alcoholic solvent to make a reactive derivative of compound (137) and reacting it with compound (266) in an alcoholic solvent. The reaction is performed as in the aforementioned step B4 in process B.

5 Step T'4 is for producing compound (268) and implemented by reacting compound (267) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step A5 in process A.

10 Step T'5 is for producing compound (269) and implemented by reacting compound (268) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A8 in process A.

15 Step T'6 is for producing compound (270) and implemented by reacting compound (269) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A9 in process A.

20 Step T'7 is an alternative method for producing compound (270) and implemented by reacting compound (268) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A9 in process A.

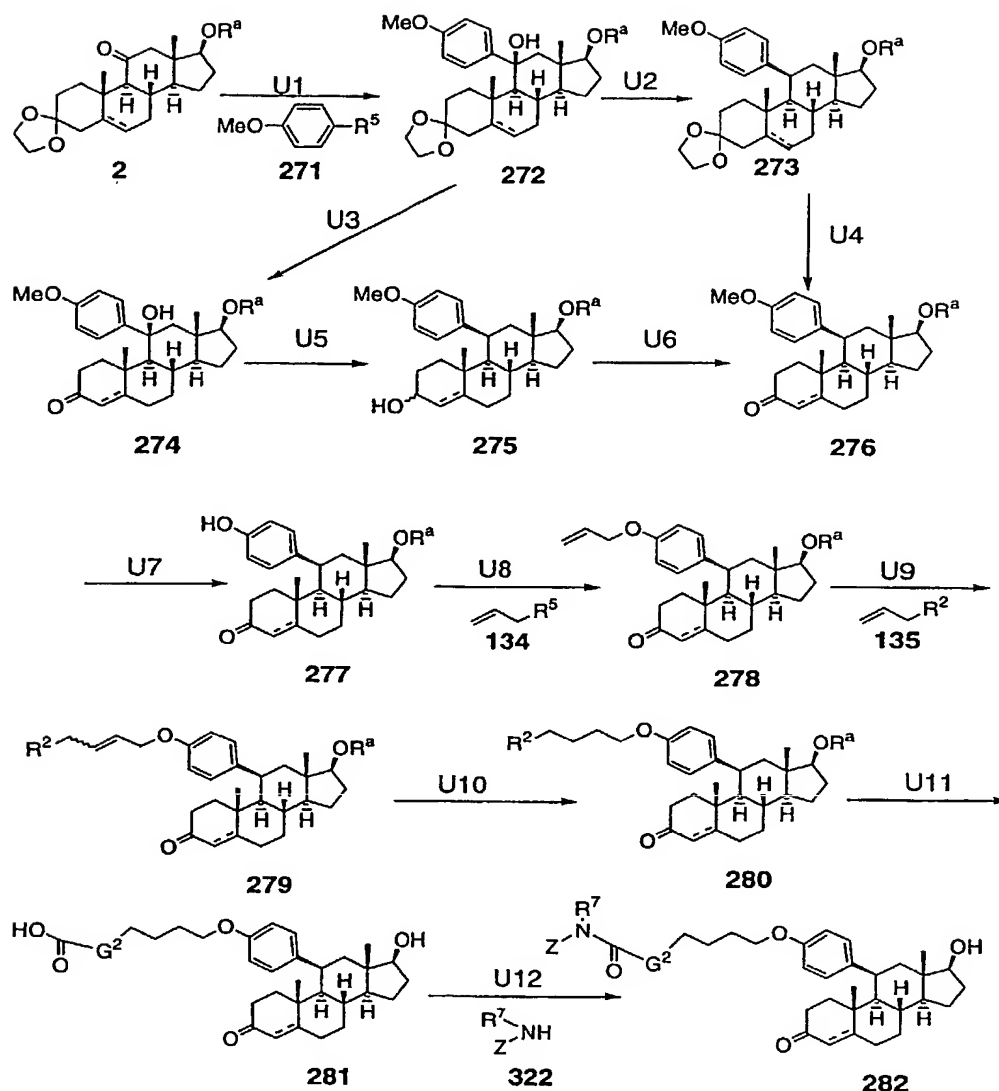
25 In process T', step T'3 and step T'4 may be interchanged in their sequence. If desired, step T'4 and step T'5 may also be interchanged in their sequence. Compound (270) can also be obtained from compound (267) if the sequence of reaction steps is T'6 → T'4.

Process U is for producing compound (276) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula

(II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R¹ is a methyl group, X² is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond; compound (278) represented by the general formula (I) in which X¹ is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R¹ is -CH₂-CH=CH₂, X² is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond; compound (279) represented by the general formula (I) in which X¹ is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R¹ is -CH₂-CH=CH-CH₂-R², X² is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond; compound (280) represented by the general formula (I) in which X¹ is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R¹ is -CH₂-CH₂-CH₂-CH₂-R², X² is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-

position to which they are bound, are $-(C=O)$, and the dashed line together with the solid line is a single bond or a double bond; compound (281) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is $-O-$ and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{COOH}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond; and compound (282) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is $-O-$ and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{CON}(R^7)Z$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond

Process U



Step U1 is for producing compound (272) and implemented by reacting compound (271) with a metal (preferably magnesium) or an alkyllithium (preferably n-butylolithium) in an inert solvent to make a reactive derivative of compound (271) and reacting it with compound (2) in an inert solvent. The reaction is performed as in the aforementioned step I1 in process I.

Step U2 is for producing compound (273) and

implemented by reacting compound (272) with a reducing agent in an inert solvent in the presence of an additive. The reaction is performed as in the aforementioned step E2 in process E.

- 5 Step U3 is for producing compound (274) and implemented by reacting compound (272) with an acid in an aqueous solvent.

 The solvent to be used is not limited in any particular way as long as it does not interfere with the
10 reaction; examples are mixtures of water and ether solvents such as ether, tetrahydrofuran and dioxane, alcoholic solvents such as methanol and ethanol, or ketonic solvents such as acetone, and hydrous acetone is preferred.

 The acid to be used may be exemplified by inorganic
15 acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid and phosphoric acid, and organic acids such as acetic acid, p-toluenesulfonic acid and pyridinium-p-toluenesulfonate, with hydrochloric acid being preferred. The reaction temperature which varies
20 with the type of solvent and the like is typically in the range of 0°C - 50°C (preferably 10°C - 30°C). The reaction time which varies with the reaction temperature and the like is typically in the range of 15 minutes - 24 hours (preferably 30 minutes - 5 hours).

- 25 Step U4 is for producing compound (276) and implemented by reacting compound (273) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step U3 in process U.

Step U5 is for producing compound (275) and implemented by reacting compound (274) with a reducing agent in an inert solvent in the presence of an additive. The reaction is performed as in the aforementioned step E2
5 in process E.

Step U6 is an alternative method for producing compound (276) and implemented by reacting compound (275) with an oxidizing agent in an inert solvent.

The inert solvent to be used is not limited in any
10 particular way as long as it does not interfere with the reaction; examples are halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, ethers such as tetrahydrofuran, dioxane and dimethoxyethane, and hydrocarbon solvents such as benzene, toluene, xylene,
15 quinoline and chlorobenzene, with dichloromethane and tetrahydrofuran being preferred. Water may optionally be added to these solvents. The oxidizing agent to be used is not limited in any particular way and examples can be manganese compounds such as potassium permanganate,
20 manganese dioxide, manganese(III) acetate, tris(acetonilacetonite)manganese(III) (MTA), manganese sulfate and manganese(III) pyrophosphate, chromates such as chromium(IV) oxide, Jones reagent, Sarett reagent, Collins reagent, chromic acid t-butyl ester, potassium bichromate,
25 Beckmann's mixture, sodium bichromate, Kiliani reagent, chromyl chloride, chromyl acetate, pyridinium chlorochromate (PCC), and pyridinium dichromate (PDC); ruthenium compounds such as ruthenium tetroxide,

- tris(triphenylphosphine)dichlororuthenium/iodosylbenzene,
 tris(triphenylphosphine)dichlororuthenium/N-
 methylmorpholin-N-oxide,
 tris(triphenylphosphine)dichlororuthenium/t-butyl
- 5 hydroperoxide, tetrapropylammonium perruthenate (TPAP),
 tetrapropylammonium perruthenate (TPAP)/N-methylmorpholin-
 N-oxide, tetrabutylammonium perruthenate (TBAP), and
 tetrabutylammonium perruthenate (TBAP)/N-methylmorpholin-N-
 oxide; halogens such as hypochlorous acid, sodium
- 10 hypochlorite, potassium hypobromite, potassium hypoiodite,
 sodium chlorate, potassium chlorate, sodium bromate,
 potassium bromate, sodium iodate, potassium iodate,
 perchloryl fluoride, orthoperiodic acid, sodium
 metaperiodate, potassium metaperiodate, N-bromoacetamide,
- 15 N-bromosuccinimide and N-bromophthalimide; as well as
 dimethyl sulfoxide/oxalyl chloride; preferred examples are
 chromates such as pyridinium chlorochromate (PCC) and
 pyridinium dichromate (PDC), and ruthenium compounds such
 tetrapropylammonium perruthenate (TPAP)/N-methylmorpholin-
- 20 N-oxide. The reaction temperature which varies with the
 type of solvent and the like is typically in the range of
 -30°C ~ 100°C, preferably 0°C - 30°C. The reaction time
 which varies with the reaction temperature and the like is
 typically in the range of 10 minutes - 48 hours, preferably
- 25 30 minutes - 24 hours.

Step U7 is an alternative method of producing compound (277) and implemented by reacting compound (276) with a deprotecting agent in an inert solvent.

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atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond; compound (285)

5 represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is $-O-$ and R^1 is $-\text{CH}_2-\text{CH}=\text{CH}-\text{G}^3-\text{S}-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom,

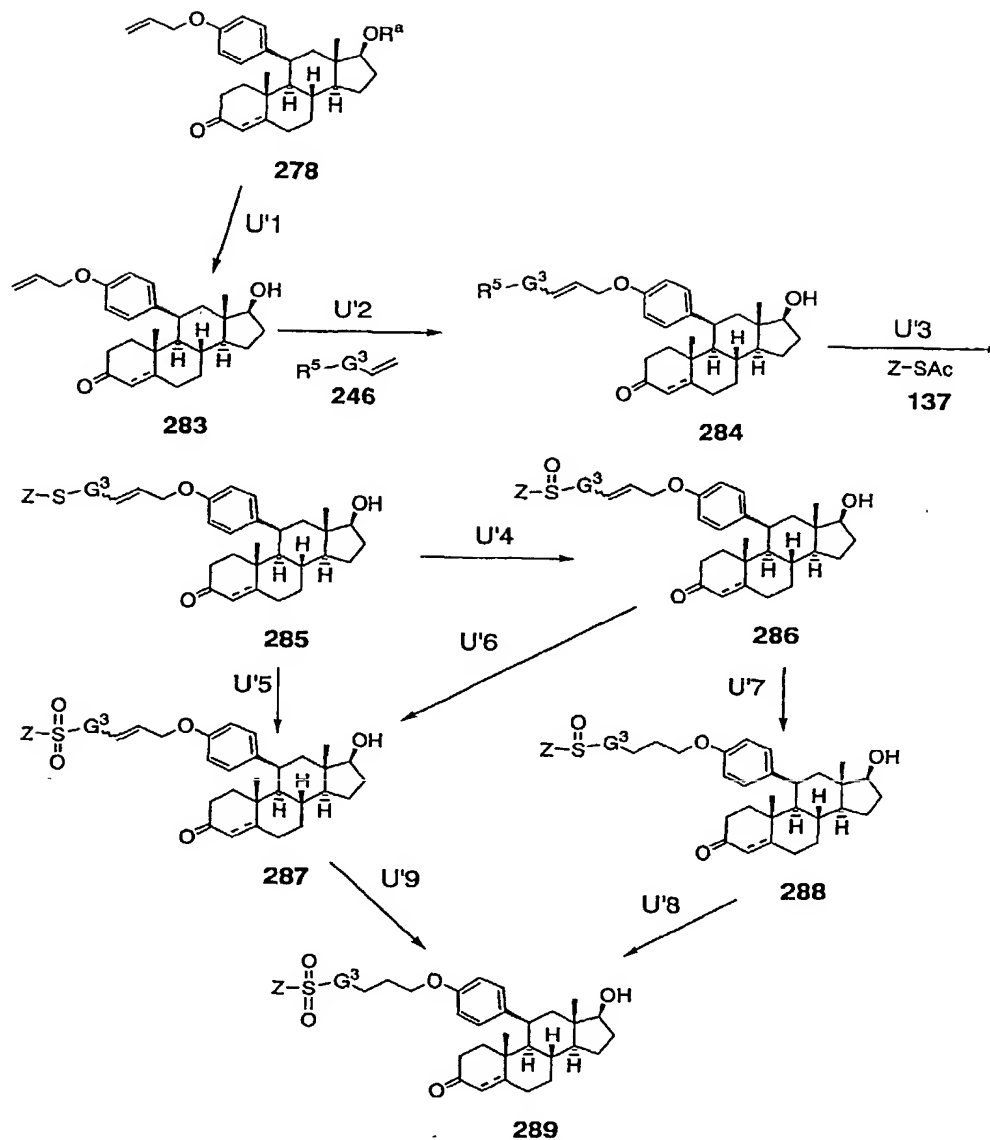
10 R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond; compound (286) represented by the general formula (I) in which X^1 is a group of β configuration that

15 is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is $-O-$ and R^1 is $-\text{CH}_2-\text{CH}=\text{CH}-\text{G}^3-\text{SO}-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they

20 are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond or a double bond; compound (287) represented by the general formula (I) in which X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon

25 group (preferably a p-phenylene group), A is $-O-$ and R^1 is $-\text{CH}_2-\text{CH}=\text{CH}-\text{G}^3-\text{SO}_2-\text{Z}$, X^2 is a hydrogen atom, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the

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Step U'1 is for producing compound (283) and implemented by reacting compound (278) with an acid in an aqueous solvent. The reaction is performed as in the
5 aforementioned step A5 in process A.

Step U'2 is for producing compound (284) and implemented by reacting compound (246) with compound (283) in an inert solvent in the presence of an organometallic

catalyst. The reaction is performed as in the
aforementioned step A4 in process A.

Step U'3 is for producing compound (285) and
implemented by reacting compound (137) with a metal
5 alkoxide in an alcoholic solvent to make a reactive
derivative of compound (137) and then reacting it with
compound (284) in an alcoholic solvent. The reaction is
performed as in the aforementioned step B4 in process B.

Step U'4 is for producing compound (286) and
10 implemented by reacting compound (285) with an oxidizing
agent in an inert solvent. The reaction is performed as in
the aforementioned step A8 in process A.

Step U'5 is for producing compound (287) and
implemented by reacting compound (285) with an oxidizing
15 agent in an inert solvent. The reaction is performed as in
the aforementioned step A9 in process A.

Step U'6 is an alternative method for producing
compound (287) and implemented by reacting compound (286)
with an oxidizing agent in an inert solvent. The reaction
20 is performed as in the aforementioned step A9 in process A.

Step U'7 is for producing compound (288) and
implemented by performing catalytic reduction in an
alcoholic solvent or an inert solvent. The reaction is
performed as in the aforementioned step A6 in process A.

25 Step U'8 is an alternative method for producing
compound (289) and implemented by reacting compound (288)
with an oxidizing agent in an inert solvent. The reaction
is performed as in the aforementioned step A9 in process A.

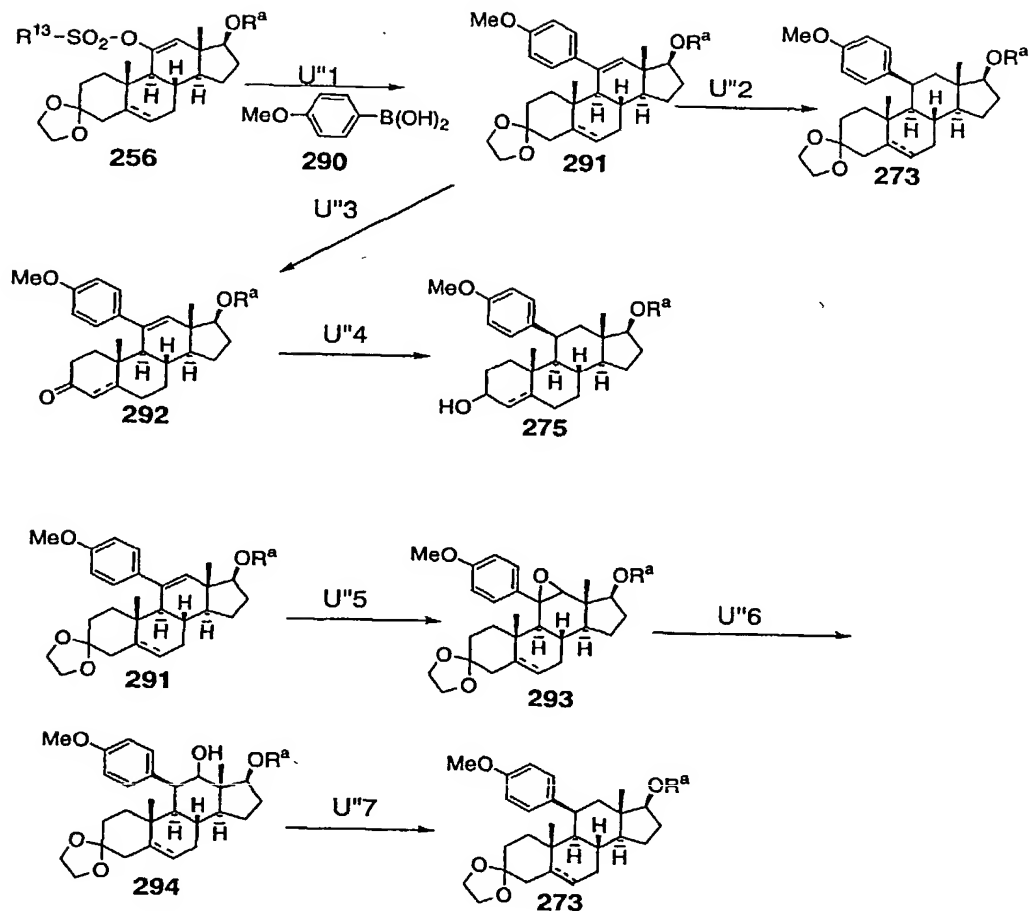
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Step U'9 is an alternative method for producing compound (289) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step A6 in process A.

In process U', compound (288) can be obtained from compound (284) if the sequence of reaction steps is $U'7 \rightarrow U'3 \rightarrow U'4$. Compound (289) can also be obtained from compound (284) if the sequence of reaction steps is $U'7 \rightarrow U'3 \rightarrow U'5$.

Process U" is an alternative method to process U' for producing compound (273) and compound (275).

Process U"



Step U"1 is for producing compound (291) and implemented by reacting compound (256) with compound (290) in an optionally miscible inert solvent in the presence of a metal catalyst and a base.

The inert solvent to be used is not limited in any particular way as long as it does not interfere with the reaction; examples are ether solvents such as dioxane and tetrahydrofuran, aromatic hydrocarbon solvents such as toluene, alcoholic solvents such as ethanol, as well as dimethylformamide, dimethylacetamide and acetonitrile, with dioxane and ethanol-toluene being preferred. The metal

catalyst to be used is not limited in any particular way and may be exemplified by tetrakis(triphenylphosphine)palladium, palladium(II) acetate-triphenylphosphine,

- 5 bis(triphenylphosphine)palladium(II) chloride, etc., with tetrakis(triphenylphosphine)palladium being preferred. The base to be used is not limited in any particular way and may be exemplified by potassium phosphate, sodium carbonate, etc., with sodium carbonate being preferred.
- 10 The reaction temperature which varies with the type of solvent and the like is typically in the range of 0°C - 180°C, preferably 10°C - 120°C. The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 48 hours, preferably
- 15 30 minutes - 24 hours.

Step U² is for producing compound (273) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The solvent to be used may be exemplified by alcoholic solvents such as

20 methanol, ethanol, n-propanol, i-propanol, n-butanol, s-butanol, t-butanol, pentanol, hexanol, cyclopropanol, cyclobutanol, cyclopentanol, cyclohexanol, ethylene glycol, 1,3-propanediol, 1,4-butanediol and 1,5-pentanediol, ether solvents such as ether, tetrahydrofuran, dioxane and

25 dimethoxyethane, aromatic solvents such as benzene, toluene, xylene, quinoline and chlorobenzene, halogen-containing solvents such as dichloromethane, chloroform and carbon tetrachloride, as well as cyclohexane, dimethyl sulfoxide,

dimethylacetamide, dimethylimidazolidinone,
dimethylformamide, N-methylpyrrolidone, ethyl acetate,
acetonitrile and nitromethane; preferred examples are
ethanol, dioxane, benzene, ethyl acetate and acetonitrile.

- 5 The condition to be used in catalytic reduction is a
homogeneous system such as hydrogen-
chlorotris(triphenylphosphine)rhodium(I), hydrogen-
chlorotris(triparatolylphosphine)rhodium(I), hydrogen-
chlorotris(triparamethoxyphenylphosphine)rhodium(I),
10 hydrogen-hydridecarbonyltris(triphenylphosphine)rhodium(I),
hydrogen-rhodium(II) acetate, hydrogen-ruthenium(II)
acetate, hydrogen-
chlorohydridetris(triphenylphosphine)ruthenium(II),
hydrogen-
15 carboxylatohydridetris(triphenylphosphine)ruthenium(II),
hydrogen-hydridecarbonyltris(triphenylphosphine)iridium(I),
hydrogen-platinum(II)-tin chloride complex, hydrogen-
pentacyanocobalt(II) complex, hydrogen-tricyanobipyridine
cobalt(II) complex, hydrogen-
20 bis(dimethylglyoximato)cobalt(II) complex, hydrogen-methyl
benzoate-tricarbonylchromium complex, hydrogen-
bis(tricarbonylcyclopentadienylchromium), hydrogen-
pentacarbonyliron, hydrogen-
bis(cyclopentadienyl)dicarbonyltitanium, hydrogen-
25 hydridecarbonylcobalt complex, hydrogen-
octacarbonyldicobalt, hydrogen-hydridecarbonylrhodium,
hydrogen-chromium(III) acetylacetonato-triisobutylaluminum,
hydrogen-cobalt(II) acetylacetonato-triisobutylaluminum, or

hydrogen-nickel(II)-2-hexanoato-triethylaluminum, or an inhomogeneous system condition such as hydrogen-platinum dioxide, hydrogen-platinum/carbon, hydrogen-palladium/carbon, hydrogen-palladium hydroxide/carbon, 5 hydrogen-palladium/barium sulfate, hydrogen-palladium/calcium carbonate, hydrogen-Raney nickel, hydrogen-copper chromite, hydrogen-rhodium/carbon, hydrogen-rhodium/alumina, hydrogen-ruthenium dioxide, hydrogen-ruthenium/carbon, or hydrogen-iridium black; 10 preferred examples are hydrogen-palladium hydroxide/carbon, hydrogen-iridium black, etc.

The reaction temperature is typically in the range of 0°C - 100°C, preferably 0°C - 60°C. The reaction time which varies with the reaction temperature and the like is 15 typically in the range of 10 minutes - 100 hours, preferably 10 minutes - 96 hours.

Step U"3 is for producing compound (292) and implemented by reacting compound (291) with an acid in an aqueous solvent. The reaction is performed as in the 20 aforementioned step U3 in process U.

Step U"4 is for producing compound (275) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step U"2 in process U".

25 Step U"5 is for producing compound (293) and implemented by reacting compound (291) with an oxidizing agent in an inert solvent.

The inert solvent to be used is not limited in any

particular way as long as it does not interfere with the reaction and examples include ether solvents such as dioxane and tetrahydrofuran, aromatic hydrocarbon solvents such as toluene, halogen-containing solvents such as dichloromethane, as well as dimethylformamide, dimethyl acetamide and acetonitrile; a preferred example is dichloromethane. The oxidizing agent to be used is not limited in any particular way and can be perbenzoic acid, metachloroperbenzoic acid, p-nitroperbenzoic acid, monoperoxyphthalic acid, performic acid, peracetic acid, trifluoroperacetic acid, etc.; a preferred example is metachloroperbenzoic acid. The reaction temperature which varies with the type of solvent and the like is typically in the range of -10°C ~ 50°C , preferably 0°C ~ 30°C . The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 48 hours, preferably 30 minutes - 24 hours.

Step U"6 is for producing compound (294) and implemented by reacting compound (293) with a reducing agent in an inert solvent.

The inert solvent to be used is not limited in any particular way as long as it does not interfere with the reaction; examples are ether solvents such as tetrahydrofuran.

The reducing agent to be used can be sodium/liquid ammonia, lithium/liquid ammonia, lithium/methylamine, lithium/ethylamine, lithium/ethylenediamine, sodium/hexamethylphosphamide-t-butanol, sodium/ethanol,

sodium/t-butanol-tetrahydrofuran, sodium/toluene-t-amyl alcohol, etc.; sodium/liquid ammonia is preferred. The reaction temperature which varies with the type of solvent and the like is typically in the range of $-100^{\circ}\text{C} \sim 20^{\circ}\text{C}$, preferably $-80^{\circ}\text{C} \sim 0^{\circ}\text{C}$. The reaction time which varies with the reaction temperature and the like is typically in the range of 10 minutes - 24 hours, preferably 30 minutes - 5 hours.

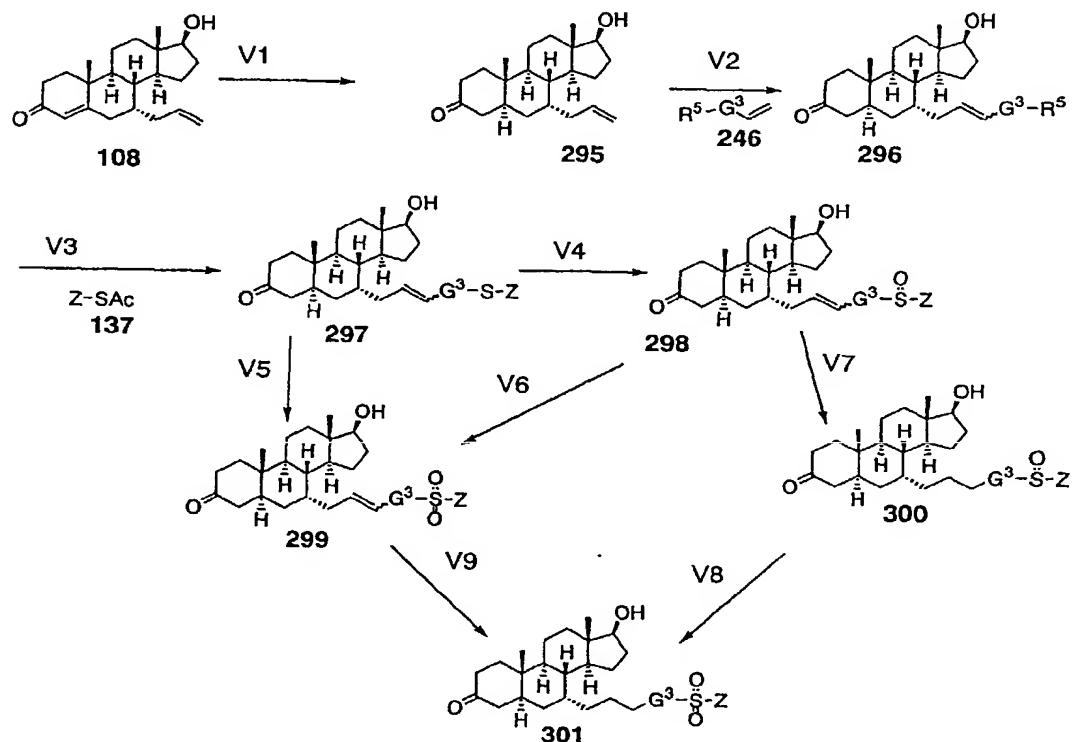
Step U"7 is an alternative method for producing
10 compound (273) and implemented by reacting compound (294)
with a reducing agent in an inert solvent in the presence
of an additive. The reaction is performed as in the
aforementioned step E2 in process E.

Process V is for producing compound (296) represented
15 by the general formula (I) in which X^1 is a hydrogen atom,
 X^2 is a group of α configuration that is represented by the
general formula (II) in which Ar is a single bond, A is a
methylene group and R^1 is $-\text{CH}-\text{CH}=\text{G}^3-\text{R}^5$, R^a is a hydrogen atom,
 R^b and R^c , when taken together with the carbon atom in 3-
20 position to which they are bound, are $-(\text{C}=\text{O})-$, and the
dashed line together with the solid line is a single bond;
compound (297) represented by the general formula (I) in
which X^1 is a hydrogen atom, X^2 is a group of α
configuration that is represented by the general formula
25 (II) in which Ar is a single bond, A is a methylene group
and R^1 is $-\text{CH}-\text{CH}=\text{G}^3-\text{S}-\text{Z}$, R^a is a hydrogen atom, R^b and R^c ,
when taken together with the carbon atom in 3-position to
which they are bound, are $-(\text{C}=\text{O})$, and the dashed line

together with the solid line is a single bond; compound (298) represented by the general formula (I) in which X^1 is a hydrogen atom, X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}=\text{CH}-\text{G}^3-\text{SO}-\text{Z}$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})$, and the dashed line together with the solid line is a single bond; compound (299) represented by the general formula (I) in which X^1 is a hydrogen atom, X^2 is a group of α configuration represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}=\text{CH}-\text{G}^3-\text{SO}_2-\text{Z}$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})$, and the dashed line together with the solid line is a single bond; compound (300) represented by the general formula (I) in which X^1 is a hydrogen atom and X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{CH}_2-\text{G}^3-\text{SO}-\text{Z}$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond; and compound (301) represented by the general formula (I) in which X^1 is a hydrogen atom and X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group

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implemented by reacting compound (246) with compound (295) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the

aforementined step A4 in process A.

Step V3 is for producing compound (297) and implemented by reacting compound (137) with a metal alkoxide in an alcoholic solvent to make a reactive
5 derivative of compound (137) and reacting it with compound (296) in an alcoholic solvent. The reaction is performed as in the aforementioned step B4 in process B.

Step V4 is for producing compound (298) and implemented by reacting compound (297) with an oxidizing
10 agent in an inert solvent. The reaction is performed as in the aforementioned step A8 in process A.

Step V5 is for producing compound (299) and implemented by reacting compound (297) with an oxidizing agent in an inert solvent. The reaction is performed as in
15 the aforementioned step A9 in process A.

Step V6 is an alternative method for producing compound (299) and implemented by reacting compound (298) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A9 in process A.

20 Step V7 is for producing compound (300) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step A6 in process A.

Step V8 is an alternative method for producing
25 compound (301) and implemented by reacting compound (300) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A9 in process A.

Step V9 is an alternative method of forming compound

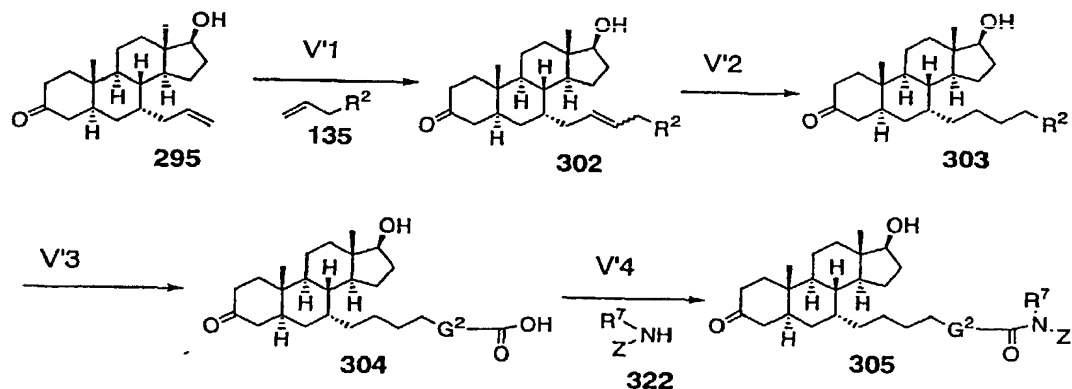
(301) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step A6 in process A.

In process V, compound (300) can be obtained from
 5 compound (296) if the sequence of reaction steps is $V7 \rightarrow V3 \rightarrow V4$. Compound (301) can also be obtained from compound (300) if the sequence of reaction steps is $V7 \rightarrow V3 \rightarrow V5$.

Process V' is for producing compound (302) represented by the general formula (I) in which X^1 is a hydrogen atom,
 10 X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}=\text{CH}-\text{CH}_2-\text{R}^2$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the
 15 dashed line together with the solid line is a single bond; compound (303) represented by the general formula (I) in which X^1 is a hydrogen atom, X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group
 20 and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{R}^2$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})$, and the dashed line together with the solid line is a single bond; compound (304) represented by the general formula (I) in which X^1 is
 25 a hydrogen atom, X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is a single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{COOH}$, R^a is a hydrogen atom, R^b and R^c , when taken

together with the carbon atom in 3-position to which they
are bound, are $-(C=O)$, and the dashed line together with
the solid line is a single bond; and compound (305)
represented by the general formula (I) in which X^1 is a
5 hydrogen atom and X^2 is a group of α configuration that is
represented by the general formula (II) in which Ar is a
single bond, A is a methylene group and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-$
 $\text{G}^2-\text{CON}(\text{R}^7)\text{Z}$, R^a is a hydrogen atom, R^b and R^c , when taken
together with the carbon atom in 3-position to which they
10 are bound, are $-(C=O)-$, and the dashed line together with
the solid line is a single bond.

Process V'



Step V'1 is for producing compound (302) and
15 implemented by reacting compound (135) with compound (295)
in an inert solvent in the presence of an organometallic
catalyst. The reaction is performed as in the
aforementioned step A4 in process A.

Step V'2 is for producing compound (303) and
20 implemented by performing catalytic reduction in an



5 implemented by hydrolyzing compound (303) in water or a water-soluble solvent in the presence of a base or an acid (preferably a base). The reaction is performed as in the aforementioned step O6 in process O.

15 Process W is for producing compound (308) represented
by the general formula (I) in which X^1 is a hydrogen atom,
 X^2 is a group of α configuration that is represented by the
general formula (II) in which Ar is an aromatic hydrocarbon
group (preferably a p-phenylene group), A is -O- and R^1 is
20 a methyl group, R^a is a hydrogen atom, R^b and R^c , when taken
together with the carbon atom in 3-position to which they
are bound, are -(C=O)-, and the dashed line together with
the solid line is a double bond; compound (309) represented
by the general formula (I) in which X^1 is a hydrogen atom,
25 X^2 is a group of α configuration that is represented by the
general formula (II) in which Ar is an aromatic hydrocarbon
group (preferably a p-phenylene group), A is -O- and R^1 is
a methyl group, R^a is a hydrogen atom, R^b and R^c , when taken

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α configuration represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{SO}-\text{Z}$, R^a is a hydrogen atom, R^b and R^c , when taken together with
5 the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})$, and the dashed line together with the solid line is a single bond; compound (315) represented by the general formula (I) in which X^1 is a hydrogen atom, X^2 is a group of α configuration represented by the general formula (II) in
10 which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{SO}_2-\text{Z}$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})$, and the dashed line together with the solid line is
15 a single bond; compound (316) represented by the general formula (I) in which X^1 is a hydrogen atom, X^2 is a group of α configuration represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{COOH}$,
20 R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})$, and the dashed line together with the solid line is a single bond; and compound (317) represented by the general formula (I) in which X^1 is a hydrogen atom and X^2 is
25 a group of α configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^2-\text{CON}(\text{R}^7)\text{Z}$, R^a is a hydrogen atom, R^b and R^c ,

1. The first part of the report

Process W



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butyllithium) in an inert solvent to make a reactive derivative of compound (307) and reacting it with compound (306) in an inert solvent in the presence of an additive (preferably tetrakis[(tri-n-butylphosphine)copper(I) iodide]). The reaction is performed as in the
5 aforementioned step O1 in process O.

Step W2 is for producing compound (309) and implemented by reacting compound (308) with a reducing agent in an inert solvent. The reaction is performed as in
10 the aforementioned step U"6 in process U".

Step W3 is for producing compound (310) and implemented by reacting compound (309) with a deprotecting agent in an inert solvent. The reaction is performed as in the aforementioned step U7 in process U.

15 Step W4 is for producing compound (311) and implemented by reacting compound (310) with a base in an inert solvent to make a salt of compound (310) and then reacting it with compound (134) in an inert solvent. The reaction is performed as in the aforementioned step A3 in
20 process A.

Step W5 is for producing compound (312) and implemented by reacting compound (135) with compound (311) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the
25 aforementioned step A4 in process A.

Step W6 is for producing compound (313) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is

performed as in the aforementioned step A6 in process A.

Step W7 is for producing compound (314) in the case where R^2 in compound (313) is G^2-S-Z and this is implemented by reacting compound (313) with an oxidizing agent in an inert solvent. The reaction is performed as in the
5 aforementioned step A8 in process A.

Step W8 is for producing compound (315) in the case where R^2 in compound (313) is G^2-S-Z and this is implemented by reacting compound (313) with an oxidizing agent in an inert solvent. The reaction is performed as in the
10 aforementioned step A9 in process A.

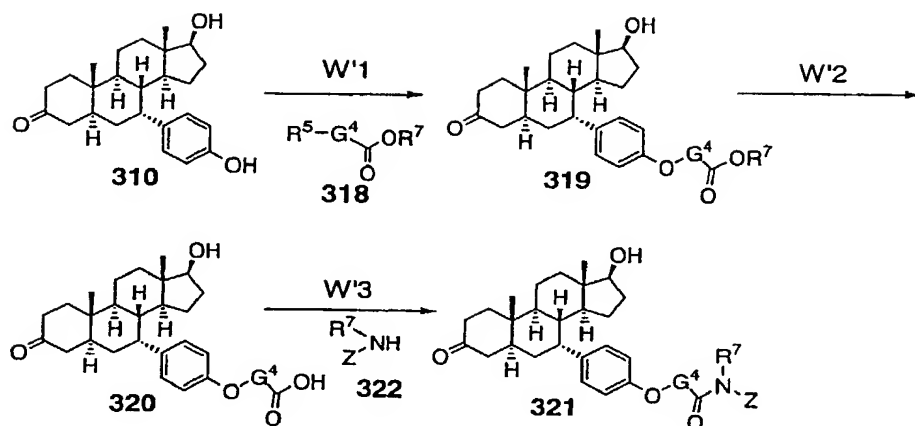
Step W10 is for producing compound (316) in the case where R^2 in compound (313) is G^2-COOR^7 and this is implemented by hydrolyzing compound (313) with a base or an acid (preferably a base) in water or a water-soluble
15 solvent. The reaction is performed as in the aforementioned step O6 in process O.

Step W11 is for producing compound (317) and implemented by reacting compound (316) or reactive derivatives thereof (acid halides, mixed acid anhydrides or
20 active esters) with compound (322) or acid addition salts thereof in an inert solvent. The reaction is performed as in the aforementioned step C3 in process C.

Process W' is for producing compound (319) represented
25 by the general formula (I) in which X^1 is a hydrogen atom, X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is

-G⁴-COOR⁷, R^a is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O), and the dashed line together with the solid line is a single bond; compound (320) represented
5 by the general formula (I) in which X¹ is a hydrogen atom, X² is a group of α configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R¹ is -G⁴-COOH, R^a is a hydrogen atom, R^b and R^c, when taken
10 together with the carbon atom in 3-position to which they are bound, are -(C=O), and the dashed line together with the solid line is a single bond; and compound (321) represented by the general formula (I) in which X¹ is a hydrogen atom and X² is a group of α configuration that is
15 represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R¹ is -G⁴-CON(R⁷)Z, R^a is a hydrogen atom, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the
20 dashed line together with the solid line is a single bond.

Process W'



Step W'1 is for producing compound (319) and implemented by reacting compound (310) with a base in an inert solvent to make a salt of compound (310) and then reacting it with compound (318) in an inert solvent. The reaction is performed as in the aforementioned step A3 in process A.

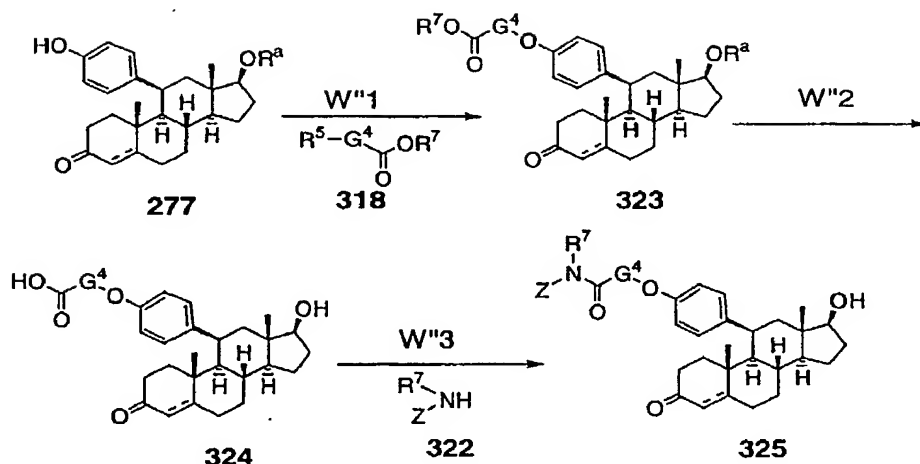
Step W'2 is for producing compound (320) and implemented by hydrolyzing compound (319) with a base or an acid (preferably a base) in water or a water-soluble solvent. The reaction is performed as in the aforementioned step O6 in process O.

Step W'3 is for producing compound (321) and implemented by reacting compound (320) or reactive derivatives thereof (acid halides, mixed acid anhydrides or active esters) with compound (322) or acid addition salts thereof in an inert solvent. The reaction is performed as in the aforementioned step C3 in process C.

Process W" is for producing compound (323) represented by the general formula (I) in which X² is a hydrogen atom,

X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is - G^4 -COOR⁷, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond; compound (324) represented by the general formula (I) in which X^2 is a hydrogen atom, X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is - G^4 -COOR⁷, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond; and compound (325) represented by the general formula (I) in which X^2 is a hydrogen atom and X^1 is a group of β configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is - G^4 -CON(R^7)Z, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are -(C=O)-, and the dashed line together with the solid line is a single bond or a double bond.

25 Process W"



Step $W''1$ is for producing compound (323) and implemented by reacting compound (277) with a base in an inert solvent to make a salt of compound (277) and then reacting it with compound (318) in an inert solvent. The reaction is performed as in the aforementioned step A3 in process A.

Step $W''2$ is for producing compound (324) and implemented by reacting compound (323) with an acid in an aqueous solvent. The reaction is performed as in the aforementioned step A5 in process A.

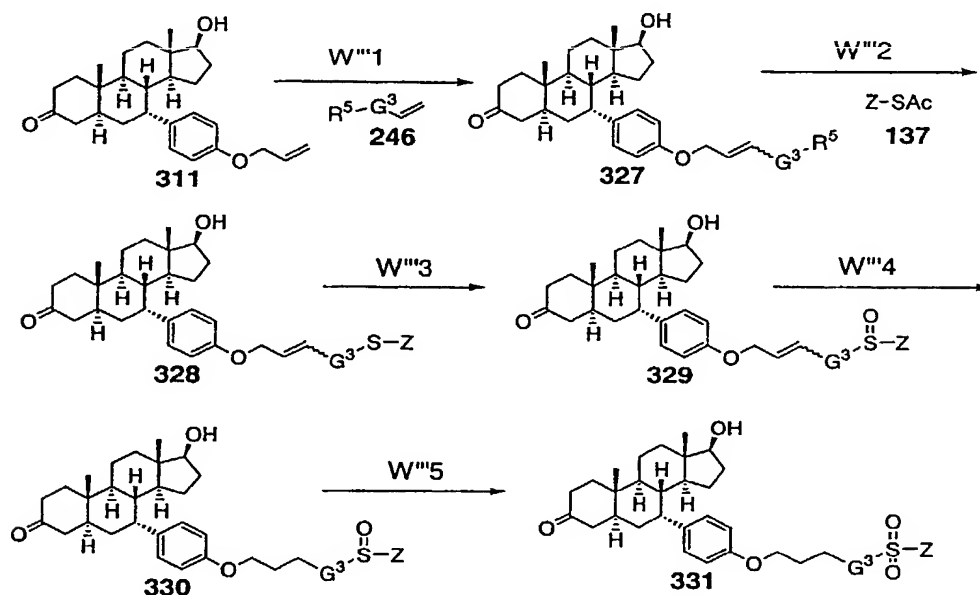
Step $W''3$ is for producing compound (325) and implemented by reacting compound (324) or reactive derivatives thereof (acid halides, mixed acid anhydrides or active esters) with compound (322) or acid addition salts thereof in an inert solvent. The reaction is performed as in the aforementioned step C3 in process C.

Process W'' is for producing compound (327) represented by the general formula (I) in which X^1 is a

hydrogen atom, X^2 is a group of α configuration represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is $-\text{CH}_2-\text{CH}=\text{CH}-\text{G}^3-\text{R}^5$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})$, and the dashed line together with the solid line is a single bond; compound (328) represented by the general formula (I) in which X^1 is a hydrogen atom and X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group, A is -O- and R^1 is $-\text{CH}_2-\text{CH}=\text{CH}-\text{G}^3-\text{S}-\text{Z}$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})-$, and the dashed line together with the solid line is a single bond; compound (329) represented by the general formula (I) in which X^1 is a hydrogen atom, X^2 is a group of α configuration represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is $-\text{CH}_2-\text{CH}=\text{CH}-\text{G}^3-\text{SO}-\text{Z}$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(\text{C}=\text{O})$, and the dashed line together with the solid line is a single bond; compound (330) represented by the general formula (I) in which X^1 is a hydrogen atom, X^2 is a group of α configuration represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is -O- and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^3-\text{SO}-\text{Z}$, R^a is a hydrogen atom, R^b and R^c , when taken

together with the carbon atom in 3-position to which they are bound, are $-(C=O)$, and the dashed line together with the solid line is a single bond; and compound (331) represented by the general formula (I) in which X^1 is a hydrogen atom and X^2 is a group of α configuration that is represented by the general formula (II) in which Ar is an aromatic hydrocarbon group (preferably a p-phenylene group), A is $-O-$ and R^1 is $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{G}^3-\text{SO}_2-\text{Z}$, R^a is a hydrogen atom, R^b and R^c , when taken together with the carbon atom in 3-position to which they are bound, are $-(C=O)-$, and the dashed line together with the solid line is a single bond.

Process W' "



Step W' "1 is for producing compound (327) and implemented by reacting compound (246) with compound (311) in an inert solvent in the presence of an organometallic catalyst. The reaction is performed as in the

aforementioned step A4 in process A.

Step W'"2 is for producing compound (328) and implemented by reacting compound (137) with a metal alkoxide in an alcoholic solvent to make a reactive derivative of compound (137) and then reacting it with compound (327) in an alcoholic solvent. The reaction is performed as in the aforementioned step B4 in process B.

Step W'"3 is for producing compound (329) and implemented by reacting compound (328) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A8 in process A.

Step W'"4 is for producing compound (330) and implemented by performing catalytic reduction in an alcoholic solvent or an inert solvent. The reaction is performed as in the aforementioned step A6 in process A.

Step W'"5 is an alternative method of producing compound (331) and implemented by reacting compound (330) with an oxidizing agent in an inert solvent. The reaction is performed as in the aforementioned step A9 in process A.

In process W'", compound (330) can also be obtained from compound (327) if the sequence of reaction steps is W'"4 → W'"2 → W'"3. Compound (331) can also be obtained from compound (327) if the sequence of reaction steps is W'"4 → W'"2 → W'"5. Compound (331) can also be obtained from compound (329) if the sequence of reaction steps is W'"5 → W'"4.

In the above-described processes A - W, B' - L', S' - W', U", W" and W'", if G and/or J and/or Q² is a group

containing a carboxyl group protected by a straight-chained
or branched lower alkyl group having 1 - 6 carbon atoms,
deprotection can easily be achieved by any known methods of
hydrolysis to effect conversion to a carboxyl-containing
5 group.

If any of the steps in the above-described processes A
- W, B' - L', S' - W', U", W" and W'" involves groups that
need be protected and deprotected, each of them can be
protected and deprotected by methods well known to the
10 skilled artisan. For the purposes of protecting and
deprotecting, reference can be had, for example, to
"Protective Groups in Organic Synthesis", 2nd edition,
Theodora W. Green, John Wiley & Sons, Inc., 1991.

Starting material compound (1) is either known or can
15 be easily prepared by known methods or similar methods.
[See, for example, J. Med. Chem. 35(11), 2113-2129 (1992);
Synth. Commun. 24(16), 2325-2340 (1994); Steroids, 60(5),
414-422 (1995).]

Starting material compound (108) is either known or
20 can be easily prepared by known methods or similar methods.
[See, for example, Tetrahedron Letters, 29(13), 1533-1536
(1988).]

Starting material compound (96) is either readily
available as a commercial product or can be easily prepared
25 by known methods or similar methods. [See, for example, J.
Chem. Res. Miniprint, 2, 0650-0669 (1986).]

Starting material compounds (119) and (144) are
readily available as commercial products.

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methods. [See, for example, Steroids, 59, 190-195 (1994).]

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vesicles increase in weight. By checking to see if the

test substance suppresses the action of testosterone or dihydrotestosterone for increasing the weights of prostate gland and seminal vesicles, one can evaluate the antagonist action of the test substance. For this measurement, reference can be had, for example, to J. Med. Chem., 41:623-639, 1998, and Kiso to Rinsho, 29(4):877-885, 1995.

Method A-2: Measuring the agonist action

A castrated rat is continuously administered the test substance. By checking to see if the weights of the prostate gland and seminal vesicles which are androgen-responsive organs increase after the administration, one can evaluate the agonist action of the test substance. For this measurement, reference can be had, for example, Folia endocrinol., 66:597-606, 1990.

Method B: Measurement based on dimer formation of the androgen receptor

Method B-1: Measuring the action for inhibiting dimer formation

Dihydrotestosterone helps the androgen receptor form a dimer. By applying a gel shift assay to determine if the test substance inhibits the dimer formation of the androgen receptor, one can evaluate the antagonist action of the test substance. For this measurement, reference can be had, for example, to J. Biol. Chem., 268:19004-19012, 1993 and J. Biol. Chem., 270:19998-20003, 1995.

Method B-2: Measuring the action for promoting dimer formation of the androgen receptor

By applying a gel shift assay to determine if the test

substance promotes the dimer formation of the androgen receptor, one can evaluate the agonist action of the test substance. For this measurement, reference can be had, for example, to J. Biol. Chem., 268:19004-19012, 1993 and J. Biol. Chem., 270:19998-20003, 1995.

Method C: Measurement based on ornithine decarboxylase (ODC) activity

By determining whether the test substance elevates or lowers the ODC activity which is believed to reflect androgen-dependent activity, one can evaluate the agonist and antagonist actions of the test substance. For this measurement, reference can be had, for example, to Anal. Biochem., 113-352-355, 1981 and Folia endocrinol., 66:597-606, 1990.

Method D: Measurement based on androgen receptor binding activity

By applying a binding assay to determine whether the test substance inhibits the binding of the androgen receptor to androgen, one can evaluate the antagonist action of the test substance. For this measurement, reference can be had, for example, to Urology, 48:157-163, 1996, J. Biol. Chem., 270:19998-20003, 1995 and Kiso to Rinsho, 29(4):877-885, 1995.

Method E: Measurement based on the increase or decrease in the amount of the androgen receptor

Cells expressing the androgen receptor are treated with the test substance in both the presence and the absence of androgen. By measuring the change in the amount

of the androgen receptor in the cells, one can evaluate the action of the test substance in working as agonist for or antagonist against the androgen receptor. For this measurement, reference can be had, for example, to

5 Endocrinology, 129:2000-2010, 1991.

Method F: Measurement based on nuclear migration of the
androgen receptor

Cells expressing the androgen receptor are treated with the test substance in the presence or absence of
10 androgen. By applying immunohistostaining to determine the localization of the androgen receptor in the cells, one can check for the nuclear migration of the androgen receptor and determine the action of the test substance for inhibiting the nuclear migration of the androgen receptor,
15 thereby evaluating the action of the test substance as agonist and/or antagonist. For these measurements, reference can be had, for example, to J. Biol. Chem., 267:968-974, 1992.

The compounds of the invention which are represented
20 by the general formula (I) and the substances of the invention which act as antagonist against but not as agonist for the androgen receptor are potential antiandrogenic agents that do exhibit any side effects such as the development of androgen tolerance due to long-term
25 administration and/or hepatotoxicity and, hence, are expected to be useful as pharmaceutical compositions, say, therapeutics for diseases such as prostate cancer, prostatomegaly, male pattern alopecia, sexual prematurity,

acne vulgaris, seborrhea and hirsutism. If the compounds of the invention which are represented by the general formula (I) and the substances of the invention which act as antagonist against but not as agonist for the androgen receptor are preliminarily administered, the onset of diseases such as prostate cancer, prostatomegaly, male pattern alopecia, sexual prematurity, acne vulgaris, seborrhea and hirsutism can hopefully be prevented or retarded, so they are also potential preventives of these diseases.

Pharmaceutical compositions containing as an active ingredient the compounds of the invention which are represented by the general formula (I) and pharmaceutical compositions containing as an active ingredient the substances of the invention which act as antagonist against but not as agonist for the androgen receptor can be administered either orally or parenterally and oral administration is desirable. Prior to administration, such pharmaceutical compositions can be formulated as preparations suitable for the specific method of administration.

Pharmaceutical compositions containing as an active ingredient the compounds of the invention which are represented by the general formula (I) and pharmaceutical compositions containing as an active ingredient the substances of the invention which act as antagonist against but not as agonist for the androgen receptor can be formulated by customary pharmaceutical formulation

techniques and, depending on their use, can be applied as solid and liquid preparations including tablets, capsules, granules, powder, syrup, injection and ointment. Carriers and excipients for such preparations include solid or liquid substances. These may be exemplified by lactose, magnesium stearate, starch, talc, gelatin, agar, pectin, gum arabic, olive oil, sesame oil, ethylene glycol and others in common use.

In these preparations, the pharmaceutical compositions containing as an active ingredient the compounds of the invention which are represented by the general formula (I) and the pharmaceutical compositions containing as an active ingredient the substances of the invention which act as antagonist against but not as agonist for the androgen receptor are incorporated in amounts that vary with their dosage form but it is generally desirable that they be contained at concentrations of 5 - 100 wt%. The pharmaceutical compositions containing as an active ingredient the compounds of the invention which are represented by the general formula (I) and pharmaceutical compositions containing as an active ingredient the substances of the invention which act as antagonist against but not as agonist for the androgen receptor can be adjusted over a broad range depending on the kind of warm-blooded animals including human to be treated, the severity of the disease, doctor's diagnosis, etc. In terms of the active ingredient, the range is from 1 μ g to 500 mg/kg per day, preferably from 20 μ g to 100 mg/kg per day. This dose

can be administered once or several times in one or divided portions per day to month and is variable as appropriate according to the severity of the disease and at doctor's discretion.

5 Examples

Example 1: Evaluating the Agonist Action of Flutamide and Bicaltamide

Twenty-four hours before transfection, 1.0×10^5 HeLa cells were cultured in phenol red free DMEM/5% DCC-FBS on 10 12-well microplates. Five hundred nanograms/well of MMTV-Luc vector, 100 ng/well of pSG5-hAR and 5 ng/well of Renilla Luc vector were transfected into the HeLa cells. The transfection was performed in a liquid culture of the phenol red free DMEM using 3 mL/well of lipofectoamine.

15 Nine hours after the transfection, the liquid culture was replaced by phenol red free DMEM/3% DCC-FBS containing 10 mmol/L of hydroxyflutamide or bicaltamide. The transcriptional activity value was measured 48 hours after the replacement of the liquid culture. Transcriptional

20 activity was measured with a dual-luciferase reporter assay system. The transcriptional activity value was calculated as the value for firefly luciferase divided by the value for sea pansy luciferase. Hydroxyflutamide and bicaltamide exhibited more than five times the value for the case of

25 non-addition and, hence, the agonist action of hydroxyflutamide and bicaltamide was verified (Table 1).

<Table 1>

<u>Luciferase Activity (fold induction)¹⁾</u>	
Not added	1.00
10 μ mol/L of hydroxyflutamide	7.84 (> 5.0)
5 <u>10 μmol/L of bicaltamide</u>	<u>7.62 (> 5.0)</u>

1) The value with the luciferase activity value for
"not added" being taken as 1.00.

Example 2: Evaluating the Antagonist Action of Flutamide
10 and Bicaltamide

Twenty-four hours before transfection, 1.0×10^5 HeLa cells were cultured in phenol red free DMEM/5% DCC-FBS on 12-well microplates. Five hundred nanograms/well of MMTV-Luc vector, 100 ng/well of pSG5/hAR and 5 ng/well of
15 Renilla Luc vector were transfected into the HeLa cells. The transfection was performed in a liquid culture of the phenol red free DMEM using 3 mL/well of lipofectoamine. Nine hours after the transfection, the liquid culture was replaced by phenol red free DMEM/3% DCC-FBS containing
20 0.1 nmol/L of DHT and 1.0 mmol/L of hydroxyflutamide or bicaltamide. The transcriptional activity value was measured 48 hours after the replacement of the liquid culture. Transcriptional activity was measured with a dual-luciferase reporter assay system. The transcriptional
25 activity value was calculated as the value for firefly luciferase divided by the value for sea pansy luciferase. Hydroxyflutamide and bicaltamide lowered the transcriptional activity value of DHT to less than 50% and,

hence, the antagonist action of hydroxyflutamide and bicaltamide was verified (Table 2).

<Table 2>

5	<u>Luciferase Activity (relative activity)²⁾</u>
0.1 nmol/L of DHT	100
1.0 μ mol/L of hydroxyflutamide	29.0 (< 50.0)
<u>1.0 μmol/L of bicaltamide</u>	<u>32.0 (< 50.0)</u>

2) The value with the luciferase activity value of 0.1
10 nmol/L of DHT being taken as 100.

Example 3: Synthesis of 17 β -hydroxy-7 α -(7-carboxyheptyl)-
5 α -androstan-3-one

(Step 1)

15 17 β -t-butylldimethylsilyloxy-7 α -(2-propen-1-yl)-5 α -
androstan-3-one

Metallic lithium (220 mg) was added to liquid ammonia (150 ml) at -78 °C. After 5-minute stirring, 17 β -t-butylldimethylsilyloxy-7 α -(2-propen-1-yl)-4-androsten-3-one
20 (1.261 g) and a tetrahydrofuran solution (20 ml) of t-butanol (0.41 ml) were added and the mixture was stirred for 20 minutes. After adding 1,2-dibromoethane (3 ml) and ammonium chloride (30 g), the mixture was stirred at 25°C for 30 minutes. After adding water, extraction with ethyl
25 acetate was conducted. The organic layer was dried with magnesium sulfate and, after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl

acetate/n-hexane = 1/10) gave the end compound in 810.7 mg (yield, 64%).

¹H-NMR(270MHz, CDCl₃)δ: 0.01(6H, s), 0.73(3H, s), 0.88(9H, s), 1.04(3H, s), 0.92-2.45(23H, m), 3.55(1H, t, J=8.3Hz),
5 4.93(1H, d, J=3.8Hz), 4.99(1H, s), 5.58-5.72(1H, m).

Rf value (on silica gel plate, developing solvents: ethyl acetate/hexane = 1/10): 0.54

(Step 2)

17β-t-butyltrimethylsilyloxy-7α-(7-methoxycarbonyl-2-hepten-
10 1-yl)-5α-androstan-3-one

17β-t-Butyltrimethylsilyloxy-7α-(2-propen-1-yl)-5α-androstan-3-one (596.1 mg) was dissolved in dichloromethane (5 ml) and, after adding methyl 6-heptenoate (384.4 mg) and benzylidenebis(tricyclohexylphosphine)-dichlororuthenium
15 (57.0 mg), the mixture was heated under reflux for 5 hours in an argon atmosphere. After standing to cool, purification was effected by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/10) to give the end compound in 527.6 mg (yield,
20 70%).

¹H-NMR(270MHz, CDCl₃)δ: 0.01(6H, s), 0.71(3H, s), 0.88(9H, s), 1.03(3H, s), 0.90-2.10(26H, m), 2.18-2.43(5H, m), 3.51(1H, t, J=8.4Hz), 3.67(3H, s), 5.18-5.40(2H, m).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.43

(Step 3)

17β-hydroxy-7α-(7-carboxyheptyl)-5α-androstan-3-one

17β-t-Butyltrimethylsilyloxy-7α-(7-methoxycarbonyl-2-

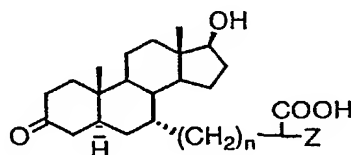
hepten-1-yl)-5 α -androstan-3-one (505.5 mg) was dissolved in ethyl acetate (30 ml) and, after adding 10%-palladium/carbon (148 mg), the mixture was stirred for 4 hours at 25°C in a hydrogen atmosphere. The reaction mixture was filtered and the solvent was distilled off at reduced pressure; the resulting residue was dissolved in acetone (10 ml) and, after adding 1 N-HCl (1 ml), the mixture was heated under reflux for 26 hours. After standing to cool, water was added and extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/2 ~ 1/1) gave the end compound in 362.6 mg (yield, 93%).

¹H-NMR(270MHz, CDCl₃) δ : 0.76(3H, s), 1.04(3H, s), 1.00-1.82(27H, m), 1.98-2.15(3H, m), 2.23-2.48(5H, m), 3.65(1H, t, J=8.7Hz).

Mass(FAB): 433(M+1).

R_f value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/1): 0.27

The following compounds were synthesized by similar methods to Example 3.



Example	n	Z	MW (Molecular weight)	Mass
4	4	H	404	405 (FAB)
5	8	H	460	461 (FAB)
6	10	H	488	489 (FAB)
7	12	H	516	517 (FAB)
8	8	$-(\text{CH}_2)_3\text{CF}_2\text{CF}_3$	620	621 (ESI)

[Example 9]

Synthesis of 17 β -hydroxy-7 α -{7-(N,N-dimethylaminocarbonyl)-heptyl}-5 α -androstan-3-one

The 17 β -hydroxy-7 α -(7-carboxyheptyl)-5 α -androstan-3-one (9.9 mg) obtained in Example 3 was dissolved in tetrahydrofuran (0.5 ml) and, after adding 1-(N,N-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (13.0 mg), 1-hydroxybenzotriazole monohydrate (10.5 mg) and a solution (68.7 μ l) of 2.0 M-dimethylamine in tetrahydrofuran, the mixture was stirred for 15 hours at 25 °C. After adding ethyl acetate (2.0 ml), the mixture was washed with 1 N-hydrochloric acid, a saturated aqueous solution of sodium hydrogencarbonate and a saturated aqueous solution of sodium chloride. After drying with magnesium sulfate, the mixture was filtered through NH silica gel (Pro. No. DM1020; product of Fuji Silicia Chemical Co., Ltd.) and the solvent was distilled off at reduced pressure to give the end compound in 10.5 mg (99.7%).

$^1\text{H-NMR}$ (270MHz, CDCl_3) δ : 0.76(3H, s), 1.04(3H, s), 1.00-1.83(27H, m), 1.95-2.16(3H, m), 2.23-2.47(5H, m), 2.94(3H,

$\frac{d}{dt} \left(\frac{\partial L}{\partial \dot{x}} \right) = \frac{\partial L}{\partial x}$

Rf value (on silica gel plate, developing solvents:
methanol/chloroform = 1/1): 0.28

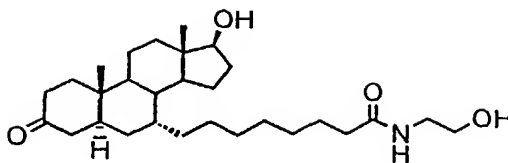
5

O=C1CC[C@]2(C)[C@@H](CCCCNC(=O)N(*)*)[C@H]3CC[C@H]2[C@@H]1C3

Example	n	RM	RN	MW	Mass
10	7	H	Et	459	460 (FAB)
11	7	H	cyclohexylmethyl	527	528 (FAB)
12	7	H	cyclopropylmethyl	485	486 (FAB)
13	7	H	n-Bu	487	488 (ESI)
14	7	H	i-Pr	473	474 (FAB)
15	7	H	t-Bu	487	488 (FAB)
16	7	H	c-hexyl	513	514 (ESI)
17	7	H	-(CH ₂) ₃ OH	489	490 (ESI)
18	7	Me	n-Bu	501	502 (ESI)
19	7	Et	Et	487	488 (ESI)
20	7	-(CH ₂) ₅ -		499	500 (ESI)
21	7	H	4-t-butylbenzyl	577	578 (ESI)
22	7	H	-CH ₂ CHPh ₂	611	612 (ESI)
23	7	H	2-furylmethyl	511	512 (ESI)
24	7	H	Me	445	446 (ESI)
25	7	Me	Et	473	474 (ESI)
26	7	Me	n-Pr	487	488 (ESI)
27	7	Me	i-Pr	487	488 (FAB)
28	7	Me	Bn	535	536 (ESI)

29	7	-(CH ₂) ₄ -		485	486 (ESI)
30	7	-CH ₂ CH ₂ OCH ₂ CH ₂ -		501	502 (ESI)
31	7	Me	t-Bu	501	502 (ESI)
32	7	H	cyclopropyl	471	472 (ESI)
33	6	Me	Me	445	446 (FAB)
34	6	Et	Et	473	474 (FAB)
35	6	-(CH ₂) ₅ -		485	486 (FAB)
36	8	Me	Me	473	474 (ESI)
37	8	Et	Et	501	524 (ESI)
38	8	Me	n-Bu	515	538 (ESI)
39	8	H	Bn	535	558 (ESI)
40	8	H	-(CH ₂) ₂ OH	489	512 (ESI)
41	8	-(CH ₂) ₅ -		513	514 (ESI)
42	9	Me	Me	487	488 (ESI)
43	9	Et	Et	515	516 (ESI)
44	9	-(CH ₂) ₄ -		513	514 (ESI)
45	9	Me	Et	501	502 (ESI)
46	9	Me	n-Bu	529	530 (ESI)
47	9	H	Bn	549	550 (ESI)
48	9	-(CH ₂) ₅ -		527	528 (ESI)
49	9	H	-(CH ₂) ₂ OH	503	504 (ESI)
50	9	Me	n-Pr	515	516 (ESI)
51	9	-CH ₂ CH ₂ OCH ₂ CH ₂ -		529	530 (ESI)
52	10	Me	Me	501	502 (FAB)
53	10	Et	Et	529	530 (FAB)
54	10	Me	Et	515	516 (FAB)
55	10	Me	n-Pr	529	530 (FAB)
56	10	Me	n-Bu	543	544 (FAB)
57	10	-CH ₂ CH ₂ OCH ₂ CH ₂ -		543	544 (FAB)
58	11	Me	Me	515	516 (FAB)
59	11	Et	Et	543	544 (FAB)
60	11	-(CH ₂) ₅ -		555	556 (FAB)
61	11	H	Bn	577	578 (FAB)
62	11	Me	n-Bu	557	558 (FAB)
63	11	H	-(CH ₂) ₂ OH	531	532 (FAB)

[Example 64]



Synthesis of 17β-hydroxy-7α-[7-{N-(2-hydroxyethyl)-aminocarbonyl}heptyl]-5α-androstan-3-one

5 The 17β-hydroxy-7α-(7-carboxyheptyl)-5α-androstan-3-one (10.3 mg) obtained in Example 3 and O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluromium hexafluorophosphate (30 mg) were dissolved in tetrahydrofuran (1 ml) and, after adding N,N-
10 diisopropylethylamine (25 μl) and 2-aminoethanol (4.4 μl), the mixture was stirred for 2 hours at 25°C. After adding ethyl acetate, the reaction mixture was washed with a saturated aqueous solution of sodium hydrogencarbonate, 1 N-hydrochloric acid and a saturated aqueous solution of
15 sodium chloride. To the organic layer, NH silica gel (Pro. No. DM1020; product of Fuji Silicia Chemical Co., Ltd.) was added and the mixture was stirred for 5 minutes; after filtering, the solvent was distilled off at reduced pressure. The resulting residue was purified by silica gel
20 column chromatography (developing solvents: methanol/chloroform = 1/10) to give the end compound in 7.5 mg (yield, 66%).

¹H-NMR(270MHz, CDCl₃)δ: 0.76(3H, s), 1.04(3H, s), 0.95-1.82(28H, m), 1.95-2.10(3H, m), 2.20(2H, t, J=7.4Hz), 2.28-

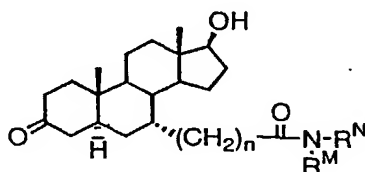
2.45(2H, m), 3.43(2H, q, J=5.2Hz), 3.60-3.78(3H, m),
5.98(1H, brs).

Mass(ESI): 476(M+1).

Rf value (on silica gel plate, developing solvents:

5 methanol/chloroform = 1/10): 0.12

The following compounds were synthesized by similar methods to Example 64.



Example	n	R ^M	R ^N	MW	Mass
65	7	H	n-Pr	473	474(FAB)
66	7	H	n-hexyl	515	516(ESI)
67	7	H	i-pentyl	501	502(FAB)
68	7	H	i-Bu	487	488(FAB)
69	7	H	neopentyl	501	502(ESI)
70	7	H	3-pentyl	501	502(ESI)
71	7	n-hexyl	n-hexyl	599	600(ESI)
72	7	H	Ph	507	508(ESI)
73	7	H	Bn	521	522(ESI)
74	7	H	-CH ₂ CH ₂ Ph	535	536(ESI)

10 [Example 75]

Synthesis of 17β-hydroxy-11β-(9-carboxynonyl)-5α-androstan-
3-one

(Step 1)

3,3-Ethylenedioxy-17 β -hydroxy-5 α -androstan-11-one

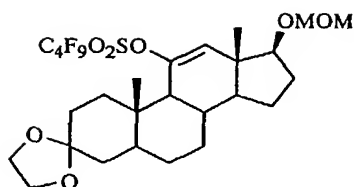
5 after adding N,N-diisopropylethylamine (2.7 ml) and
chloromethylmethyl ether (1.2 ml) dropwise, the mixture was
stirred for 8 hours at 25°C. The reaction mixture was
poured into a saturated aqueous solution of ammonium
chloride and subjected to extraction with dichloromethane.

10 The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. The resulting residue was purified by silica gel column chromatography (developing solvents:
15 ethyl acetate/n-hexane = 1/1) to give the end compound in 1.98 g (yield, 95%).

¹H-NMR(270MHz, CDCl₃)δ: 0.72(3H, s), 1.03(3H, s), 1.03-1.38(7H, m), 1.52-1.80(9H, m), 2.05-2.23(2H, m) 2.36-2.48(2H, m), 3.33(3H, s), 3.70(1H, t, J=8.4Hz), 3.92(4H, s), 4.57(1H, d, J=14.2Hz), 4.60(1H, d, J=14.2Hz).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/1): 0.61

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3,3-ethylenedioxy-17β-methoxymethoxy-11-
[{(1,1,2,2,3,3,4,4,4-nonafluorobutyl)sulfonyl}oxy]-5α-
androst-11-ene

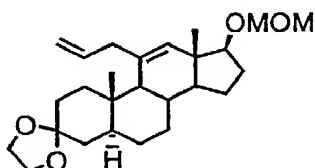
5 To a solution of lithium diisopropylamide (as prepared from diisopropylamine (0.15 ml) and n-butyllithium (1.5 M hexane solution) (0.69 ml)) in tetrahydrofuran (1.3 ml), a solution of 3,3-ethylenedioxy-17β-methoxymethoxy-5α-androstan-11-one (100 mg) in tetrahydrofuran (1.3 ml) was
10 added dropwise over 5 minutes. After stirring for 30 minutes at -78°C, perfluorobutanesulfonyl fluoride (0.13 ml) was added dropwise over 5 minutes. After stirring for 5 minutes at -78°C, the mixture was stirred for 2 hours at room temperature. A saturated aqueous solution of ammonium
15 chloride was added to the reaction mixture and extraction with ethyl acetate was effected. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure.

20 Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/6) gave the end compound in 98.8 mg (yield, 57%).

¹H-NMR(270MHz, CDCl₃)δ: 0.93(3H, s), 0.96(3H, s), 0.83-2.23(18H, m), 3.34(3H, s), 3.70(1H, t, J=8.2Hz), 3.93(4H, s), 4.58(1H, d, J=6.6Hz), 4.63(1H, d, J=6.6Hz), 6.20(1H, s).

Rf value (on silica gel plate, developing solvents: ethyl acetate/hexane = 1/2): 0.67

(Step 3)



5 3,3-ethylenedioxy-17β-(methoxymethoxy)-11-(2-propen-1-yl)-5α-androst-11-ene

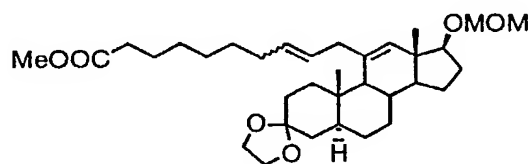
3,3-Ethylenedioxy-17β-methoxymethoxy-11-
 [{{(1,1,2,2,3,3,4,4,4-nonafluorobutyl)sulfonyl}oxy]-5α-
 androst-11-ene) (454.5 mg) was dissolved in tetrahydrofuran
 10 (6 ml) and, after adding allyltributyltin (299.1 mg),
 lithium chloride (90.0 mg) and
 tetrakis(triphenylphosphine)palladium (47.7 mg), the
 mixture was heated under reflux for 22 hours in an argon
 atmosphere. After standing to cool, an aqueous solution of
 15 potassium fluoride was added and extraction with ethyl
 acetate was effected. The organic layer was washed with
 water and a saturated aqueous solution of sodium chloride
 and dried with magnesium sulfate; after filtering, the
 solvent was distilled off at reduced pressure. The
 20 resulting residue was purified by silica gel column
 chromatography (developing solvents: ethyl acetate/n-
 hexane = 1/9) to give the end compound in 275.8 mg (yield,
 98%).

¹H-NMR(270MHz, CDCl₃)δ: 0.83(3H, s), 0.89(3H, s), 0.93-

1.88(16H, m), 1.98-2.12(2H, m), 2.72-2.92(2H, m), 3.37(3H, s), 3.59(1H, t, J=8.7Hz), 3.94(4H, s), 4.62(1H, d, J=10.1Hz), 4.65(1H, d, J=10.1Hz), 4.91-5.02(2H, m), 5.65-5.82(1H, m), 5.88(1H, s).

5 Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.53

(Step 4)



10 3,3-ethylenedioxy-17β-(methoxymethoxy)-11-(9-methoxycarbonyl-2-nonen-1-yl)-5α-androst-11-ene

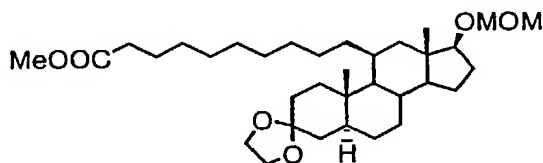
3,3-Ethylenedioxy-17β-(methoxymethoxy)-11-(2-propen-1-yl)-5α-androst-11-ene (248.5 mg) was dissolved in dichloromethane (3 ml) and, after adding methyl 8-nonenoate (202.9 mg) and benzylidenebis(tricyclohexylphosphine)-
 15 dichlororuthenium (27.3 mg), the mixture was heated under reflux for 5 hours in an argon atmosphere. After standing to cool, purification was effected by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/6) to give the end compound in 227.8 mg (yield,
 20 68%).

¹H-NMR(270MHz, CDCl₃)δ: 0.83(3H, s), 0.88(3H, s), 0.90-1.40(13H, m), 1.40-1.83(11H, m), 1.90-2.12(4H, m), 2.30(2H, t, J=7.6Hz), 2.65-2.84(2H, m), 3.36(3H, s), 3.60(1H, t, J=8.4Hz), 3.66(3H, s), 3.93(4H, s), 4.63(1H, d, J=11.2Hz),

4.65(1H, d, J=11.2Hz), 5.23-5.40(2H, m), 5.87(1H, s).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/6): 0.23

(Step 5)



5

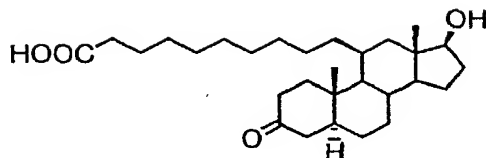
3,3-ethylenedioxy-17β-(methoxymethoxy)-11-(9-methoxycarbonylnonyl)-5α-androstane

3,3-Ethylenedioxy-17β-(methoxymethoxy)-11-(9-methoxycarbonyl-2-nonen-1-yl)-5α-androst-11-ene (226.3 mg)
10 was dissolved in ethyl acetate (5 ml) and, after adding iridium black (55.7 mg), the mixture was stirred for 5 days at 25°C in a hydrogen atmosphere. The reaction mixture was filtered through Celite and concentrated at reduced pressure; the resulting residue was purified by silica gel
15 column chromatography (developing solvents: ethyl acetate/n-hexane = 1/10 - 1/6) to give the end compound in 165.9 mg (yield, 73%).

¹H-NMR(270MHz, CDCl₃)δ: 0.83(3H, s), 0.93(3H, s), 0.95-1.05(3H, m), 1.10-1.41(20H, m), 1.45-1.80(11H, m), 1.90-2.07(2H, m), 2.16(1H, d, J=12.5Hz), 2.30(2H, t, J=7.6Hz),
20 3.35(3H, s), 3.43(1H, t, J=8.7Hz), 3.66(3H, s), 3.93(4H, s), 4.62(2H, s).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.47

(Step 6) 32-54



17β-hydroxy-11β-(9-carboxynonyl)-5α-androstan-3-one

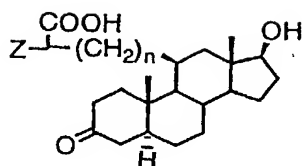
3,3-Ethylenedioxy-17β-(methoxymethoxy)-11β-(9-methoxycarbonylnonyl)-5α-androstane (91.0 mg) was dissolved in acetone (3 ml) and, after adding 1 N-hydrochloric acid (0.5 ml), the mixture was heated under reflux for 24 hours. After standing to cool, water was added and extraction with ethyl acetate was effected. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. The resulting residue was purified by silica gel column chromatography (developing solvents: ethyl acetate/chloroform = 1/6 - 1/2) to give the end compound in 70.0 mg (yield, 94%).

¹H-NMR(270MHz, CDCl₃)δ: 0.85(3H, s), 0.90-1.03(4H, m), 1.15(3H, s), 1.16-1.88(25H, m), 1.98-2.48(10H, m), 3.58(1H, t, J=8.7Hz).

Mass(FAB): 461(M+1).

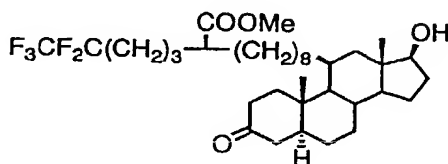
R_f value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/2): 0.086

The following compounds were synthesized by similar methods to Example 75.



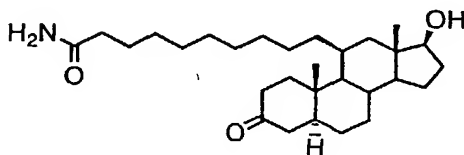
Example	n	Z	MW	Mass
76	6	H	432	433 (FAB)
77	7	H	446	447 (FAB)
78	10	H	488	489 (FAB)
79	8	$-(CH_2)_3CF_2CF_3$	620	621 (ESI)

[Example 80]



5 MW 634, Mass(ESI): 635(M+1).

[Example 81]



10 Synthesis of 17 β -hydroxy-11 β -(9-aminocarbonylnonyl)-5 α -androstan-3-one

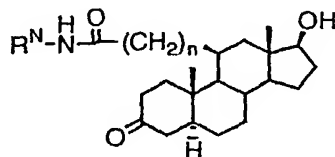
The 17 β -hydroxy-11 β -(9-carboxynonyl)-5 α -androstan-3-one (16.6 mg) obtained in Example 75 was dissolved in tetrahydrofuran (1 ml) and, after adding triethylamine (6.0 μ l) and ethyl chlorocarbonate (4.0 μ l) at -10°C, the mixture was stirred for 10 minutes. Ammonia gas was blown

into the reaction mixture for 5 minutes and the mixture was stirred for 20 minutes at -10°C . A saturated aqueous solution of ammonium chloride was added to the reaction mixture, which was then reverted to room temperature.

¹H-NMR(270MHz, CDCl₃)δ: 0.85(3H, s), 0.88-1.05(4H, m), 1.15(3H, s), 1.10-1.88(25H, m), 1.97-2.50(10H, m), 3.58(1H, t, J=8.7Hz), 5.34(2H, brs).

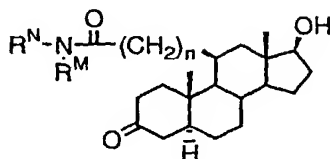
Rf value (on silica gel plate, developing solvents:
methanol/chloroform = 1/10): 0.33

The following compounds were synthesized by similar
20 methods to Example 81.



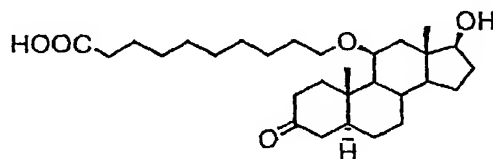
Example	n	Z	MW	Mass
82	9	n-phenyl	529	530 (FAB)
83	11	H	487	488 (FAB)
84	11	n-phenyl	557	558 (FAB)

1. The first group of people who are interested in the results of the study are the researchers themselves. They want to know if the study was successful in achieving its goals and if the data collected is reliable and valid.



Example	n	R ^M	R ^N	MW	Mass
85	7	Me	Me	459	460 (FAB)
86	7	H	Me	445	446 (FAB)
87	7	Me	Et	473	474 (FAB)
88	7	Me	n-Pr	487	488 (FAB)
89	7	-CH ₂ CH ₂ OCH ₂ CH ₂ -		501	502 (FAB)
90	8	Me	Me	473	474 (FAB)
91	8	H	Me	459	460 (FAB)
92	8	Me	Et	487	488 (ESI)
93	8	Me	n-Pr	501	502 (FAB)
94	8	-CH ₂ CH ₂ OCH ₂ CH ₂ -		515	516 (FAB)
95	9	Me	Me	487	488 (ESI)
96	9	Et	Et	515	516 (ESI)
97	9	-(CH ₂) ₅ -		527	528 (ESI)
98	9	H	Bn	549	550 (ESI)
99	9	Me	n-Bu	529	530 (ESI)
100	9	H	-CH ₂ CH ₂ OH	503	504 (ESI)

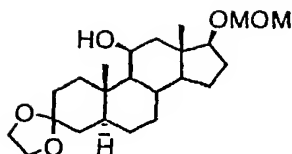
[Example 101]



5

Synthesis of 17 β -hydroxy-11 β -(9-carboxynonyloxy)-5 α -androstan-3-one

(Step 1)



3,3-ethylenedioxy-11β-hydroxy-17β-(methoxymethoxy)-5α-androstane

3,3-Ethylenedioxy-17β-(methoxymethoxy)-5α-androstan-
 5 11-one (2.84 g) was dissolved in diethyl ether (500 ml) and, after adding lithium aluminum hydride (548 mg), the mixture was heated under reflux for 2 hours in an argon atmosphere. The reaction mixture was cooled to 0°C and, after adding water, filtered through Celite. After extraction with
 10 ethyl acetate, the organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. The resulting residue was purified by silica gel column chromatography
 15 (developing solvents: ethyl acetate/n-hexane = 1/2) to give the end compound in 2.68 g (yield, 94%).

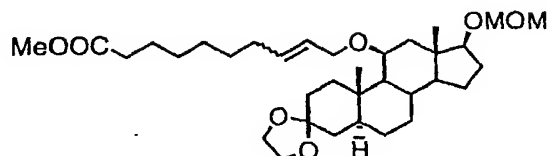
¹H-NMR(270MHz, CDCl₃)δ: 0.75-0.99(3H, m), 1.01(3H, s), 1.06(3H, s), 1.20-1.92(16H, m), 1.94-2.07(2H, m), 3.35(3H, s), 3.49(1H, t, J=8.3Hz), 3.94(4H, s), 4.29-4.36(1H, m),
 20 4.61(2H, s).

Rf value (on silica gel plate, developing solvents: methanol/chloroform = 1/50): 0.31
 (Step 2)

In an argon atmosphere, 3,3-ethylenedioxy-11 β -hydroxy-17 β -(methoxymethoxy)-5 α -androstande (953.9 mg) was dissolved in N,N-dimethylformamide (10 ml) and, after adding sodium hydride (60% in oil) (486.7 mg), the mixture was stirred for 3 hours at 50°C. After reversion to 25°C, allyl bromide (2.20 ml) and tetra-n-butylammonium iodide (208.5 mg) were added and the mixture was stirred for 3 hours at 50°C. The reaction mixture was cooled to 0°C and water was added. After extraction with ethyl acetate, the organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. The resulting residue was purified by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/5) to give the end compound in 684.5 mg (yield, 65%).

¹H-NMR(270MHz, CDCl₃) δ : 0.74-0.93(3H, m), 0.95(3H, s), 1.03(3H, s), 1.18-2.09(16H, m), 2.32(1H, dd, J=2.9, 14.4Hz), 3.36(3H, s), 3.47(1H, t, J=8.3Hz), 3.70(1H, dd, J=7.2, 16.2Hz), 3.77-3.83(1H, m), 3.93(4H, s), 4.10(1H, dd, J=7.2, 16.2Hz), 4.63(2H, AB-q), 5.08(1H, split-d, J=10.6Hz), 5.25(1H, dd, J=1.7, 17.2Hz), 5.83-6.00(1H, m).

(Step 3)

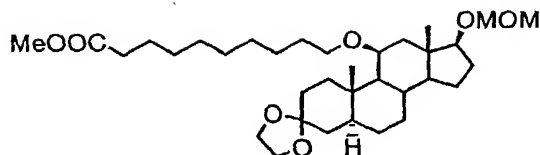


3,3-Ethylenedioxy-17 β -(methoxymethoxy)-11 β -(2-propen-1-yloxy)-5 α -androstande (18.9 mg) was dissolved in dichloromethane (0.5 ml) and, after adding methyl 8-nonenoate (14.8 mg) and benzylidenebis(tricyclohexylphosphine)-dichlororuthenium (2.0 mg), the mixture was heated under reflux for 4 hours in an argon atmosphere. After standing to cool and concentrating at reduced pressure, purification was effected by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/5) to give the end compound in 15.5 mg (yield, 62%).

1H-NMR(270MHz, CDCl₃)δ: 0.70-0.95(3H, m), 0.95(3H, s),
1.02(3H, s), 1.15-1.86(23H, m), 1.93-2.08(3H, m), 2.30(3H,
20 t, J=7.6Hz), 3.36(3H, s), 3.46(1H, t, J=8.7Hz), 3.64(1H, dd,
J=5.0, 11.3Hz), 3.67(3H, s), 3.74-3.80(1H, m), 3.93(4H, s),
4.02(1H, dd, J=5.0, 11.3Hz), 4.63(2H, AB-q), 5.44-5.69(1H,
m).

- 358 -

(Step 4)



3,3-ethylenedioxy-17β-(methoxymethoxy)-11β-(9-methoxycarbonylnonyloxy)-5α-androstane

5 3,3-Ethylenedioxy-17β-(methoxymethoxy)-11β-(9-methoxycarbonyl-2-nonen-1-yloxy)-5α-androstane (17.2 mg) was dissolved in ethyl acetate (3 ml) and, after adding 10%-palladium/carbon (6.5 mg), the mixture was stirred for 1 hour at 25 °C in a hydrogen atmosphere. The reaction

10 mixture was filtered and the solvent was distilled off at reduced pressure to give the residue in 16.7 mg. In a separate run, 3,3-ethylenedioxy-17β-(methoxymethoxy)-11β-(9-methoxycarbonyl-2-nonen-1-yloxy)-5α-androstane (32.1 mg) was dissolved in ethyl acetate (6 ml) and, after adding

15 10%-palladium/carbon (6.5 mg), the solution was stirred for 1 hour at 25°C in a hydrogen atmosphere. The reaction mixture was filtered and the solvent was distilled off at reduced pressure to give the residue in 30.1 mg. The two residues were combined and purified by silica gel column

20 chromatography (developing solvents: ethyl acetate/n-hexane = 1/2) to give the end compound in 44.7 mg (yield, 90%).

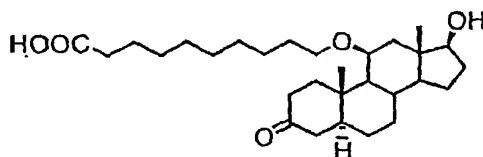
1H-NMR(270MHz, CDCl₃)δ: 0.71-0.94(3H, m), 0.94(3H, s), 1.02(3H, s), 1.20-2.07(30H, m), 2.30(3H, t, J=7.6Hz), 3.07(3H, dt, J=5.7, 8.4Hz), 3.36(3H, s), 3.43-3.58(2H, m),

25

3.67(3H, s), 3.68-3.74(1H, m), 3.93(4H, s), 4.63(2H, AB-q).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/2): 0.55

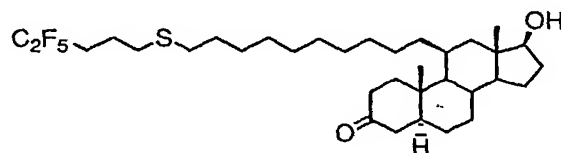
(Step 5)



5

17β-hydroxy-11β-(9-carboxynonyloxy)-5α-androstan-3-one

3,3-Ethylenedioxy-17β-(methoxymethoxy)-11β-(9-methoxycarbonylnonyloxy)-5α-androstane (21.0 mg) was dissolved in acetone (2 ml) and, after adding 1 N-
 10 hydrochloric acid (0.5 ml), the mixture was heated under reflux for 10 hours. After adding water to the reaction mixture, extraction with dichloromethane was effected and the organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium
 15 sulfate; after filtering, the solvent was distilled off at reduced pressure to give the residue in 20.6 mg. In a separate run, 3,3-ethylenedioxy-17β-(methoxymethoxy)-11β-(9-methoxycarbonylnonyloxy)-5α-androstane (22.0 mg) was dissolved in acetone (2 ml) and, after adding 1 N-
 20 hydrochloric acid (0.5 ml), the mixture was heated under reflux for 10 hours. After adding water to the reaction mixture, extraction with dichloromethane was effected and the organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium
 25 sulfate; after filtering, the solvent was distilled off at

pentafluoropentylsulfanyl)decyl)-5 α -androstan-3-one

The 3,3-diethylenedioxy-17 β -(methoxymethoxy)-11 β -(9-methoxycarbonylnonyl)-5 α -androstan-3-one (64.8 mg) obtained in
 5 step 5 of Example 75 was dissolved in tetrahydrofuran (3 ml) and, after adding lithium borohydride (11 mg), the mixture was stirred for 4 hours at 25°C. To the reaction mixture, lithium triethylborohydride (1.0 M-tetrahydrofuran solution, 100 μ l) was added and the mixture was stirred for
 10 4 hours at 25°C. To the reaction mixture, lithium borohydride (20 mg) was added and the mixture was stirred for 15 hours at 25°C. After adding water, extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and
 15 dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. The resulting residue was purified by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/4 - 1/2) to give an oil in 63.8 mg. This oil was dissolved in
 20 dichloromethane (2 ml) and, after adding triethylamine (30 μ l) and methanesulfonyl chloride (15 μ l) at 0°C, the mixture was stirred for 4 hours at 25°C. The reaction mixture was poured into a saturated aqueous solution of sodium chloride and extraction with dichloromethane was
 25 conducted. The organic layer was dried with magnesium

sulfate and after filtering, the solvent was distilled off at reduced pressure. The resulting residue was dissolved in acetone (3 ml) and, after adding sodium iodide (300 mg), the mixture was stirred for 15 hours at 25°C. A saturated aqueous solution of sodium sulfite was added to the reaction mixture and extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. The residue was purified by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/4) to give an oil in 53.9 mg. This oil and 1-(acetylsulfanyl)-4,4,5,5,5-pentafluoropentane (45 mg) were dissolved in methanol (1 ml) and tetrahydrofuran (0.5 ml) and, after adding a methanol solution (0.18 ml) of 1 N-sodium methoxide, the mixture was stirred for 15 hours at 25°C. After adding water to the reaction mixture, extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. The residue was purified by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/4) to give an oil in 66.3 mg. This oil was dissolved in acetone (2 ml) and, after adding 1 N-hydrochloric acid (0.5 ml), the mixture was heated under reflux for 36 hours. After standing to cool, water was added and extraction with ethyl acetate was



5

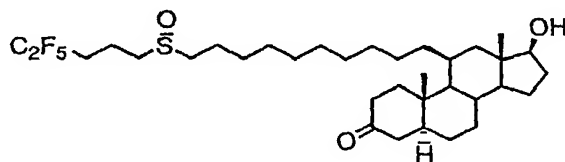
10

Mass (FAB): 623 (M+1).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.19

15

Synthesis of 17 β -hydroxy-11 β -(10-(4,4,5,5,5-pentafluoropentylsulfinyl)decyl)-5 α -androstan-3-one



20

was added to the reaction mixture and, after reverting it to room temperature, extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. The residue was purified by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/2 ~ 1/1 ~ 2/1) to give the end compound in 19.5 mg (yield, 93%).

1H-NMR(270MHz, CDCl₃)δ: 0.85(3H, s), 0.86-1.05(3H, m), 1.15(3H, s), 1.10-1.90(27H, m), 1.95-2.50(13H, m), 2.60-2.82(4H, m), 3.57(1H, t, J=8.2Hz).

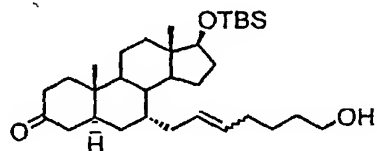
Mass(FAB): 639(M+1).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.056

[Example 111]

Synthesis of 17β-hydroxy-7α-(7-hydroxyheptyl)-5α-androstan-3-one

(Step 1)



17β-t-butyldimethylsilyloxy-7α-(7-hydroxy-2-hepten-1-yl)-5α-androstan-3-one

17β-t-Butyldimethylsilyloxy-7α-(2-propen-1-yl)-5α-androstan-3-one (33.4 mg) was dissolved in dichloromethane

after adding 2 N-hydrochloric acid (0.5 ml), the mixture was stirred for 2 hours at 25°C. After adding water to the reaction mixture, extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. The resulting residue was purified by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/2 - 1/1) to give the end compound in 15.0 mg (yield, 98%).

¹H-NMR(270MHz, CDCl₃)δ: 0.76(3H, s), 1.04(3H, s), 0.80-1.83(29H, m), 1.95-2.15(3H, m), 2.22-2.47(3H, m), 3.60-3.70(3H, m).

Mass(ESI): 405(M+1).

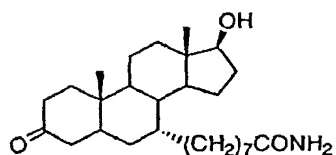
Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/1): 0.24

The following compounds were synthesized by similar methods to Example 111.

Example	n	MW	Mass (ESI)
112	8	418	419
113	9	432	433

20

[Example 114]



[Faint, illegible markings]

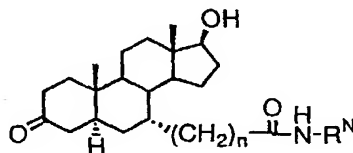
15 dichloromethane/methanol = 20/1) gave the end compound in
11.6 mg (92%).

¹H-NMR(270MHz, CDCl₃)δ: 0.76(3H, s), 1.04(3H, s), 1.00-1.83(27H, m), 1.94-2.16(3H, m), 2.20-2.50(5H, m), 3.65(1H, t, J=8.4Hz), 5.34-5.54(2H, m).

20 Mass(FAB): 432(M+1).

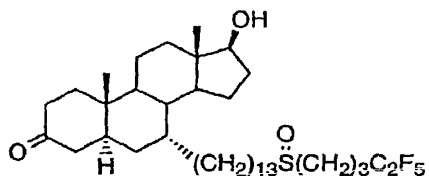
Rf value (on silica gel plate, developing solvents:
dichloromethane/methanol = 20/1): 0.48

25 methods to Example 114.

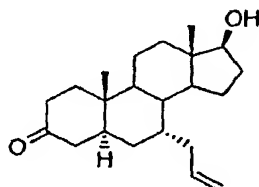


Example	n	R ^N	MW	Mass (FAB)
115	5	H	403	404
116	5	n-pentyl	473	474
117	7	n-pentyl	501	502
118	9	H	459	460
119	9	n-pentyl	529	529
120	11	H	487	487
121	11	n-pentyl	557	557
122	13	H	515	515
123	13	n-pentyl	585	585

[Example 124]



5 17β-hydroxy-7α-(13-(4,4,5,5,5-pentafluoropentylsulfinyl)-tridecyl)-5α-androstan-3-one
(Step 1)



Synthesis of 17β-hydroxy-7α-(2-propen-1-yl)-5α-androstan-3-one

10 17β-t-Butyldimethylsilyloxy-7α-(2-propen-1-yl)-5α-androstan-3-one (170 mg) was dissolved in acetone (2 ml) and then 2 N-hydrochloric acid (0.5 ml) was added dropwise. After stirring for 4 hours at 25°C, water was added to the

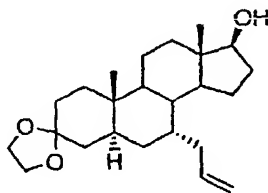
reaction mixture and extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was

5 distilled off at reduced pressure to give the end compound in 126 mg (100%).

¹H-NMR(270MHz, CDCl₃)δ: 0.77(3H, s), 1.04(3H, s), 0.96-2.44(23H, m), 3.60-3.70(1H, m), 4.94(1H, d, J=3.5Hz), 5.00(1H, s), 5.58-5.72(1H, m).

10 R_f value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/1): 0.54

(Step 2)



15 Synthesis of 3,3-ethylenedioxy-17β-hydroxy-7α-(2-propen-1-yl)-5α-androstane

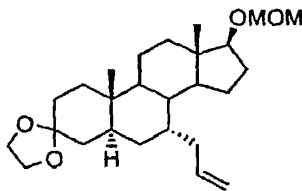
To a benzene solution (5 ml) of 17β-hydroxy-7α-(2-propen-1-yl)-5α-androstan-3-one (126 mg), ethylene glycol (2 ml) and p-toluenesulfonic acid (13.2 mg) were added and the mixture was heated under reflux with water being
20 continuously removed with a Dean-Stark trap. After two hours, a saturated aqueous solution of sodium hydrogencarbonate was added under cooling with ice and extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of

sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure to give the end compound in 141 mg (yield, 99%).

¹H-NMR(270MHz, CDCl₃)δ: 0.74(3H, s), 0.85(3H, s), 0.92-
5 2.20(23H, m), 3.56-3.70(1H, m), 3.93(4H, s), 4.92-5.04(2H, m), 5.62-5.80(1H, m).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/1): 0.60

(Step 3)



10

Synthesis of 3,3-ethylenedioxy-17β-methoxymethoxy-7α-(2-propen-1-yl)-5α-androstane

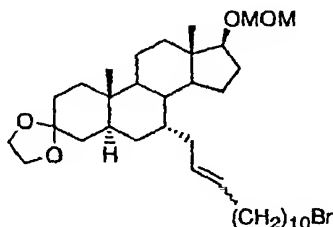
To a dichloromethane solution (4 ml) of 3,3-ethylenedioxy-17β-hydroxy-7α-(2-propen-2-yl)-5α-androstane
15 (141 mg), diisopropylethylamine (0.227 ml) and chloromethyl methyl ether (0.087 ml) were added dropwise under cooling with ice. After stirring for 14 hours at 25°C, a saturated aqueous solution of sodium hydrogencarbonate was added to the reaction mixture and extraction with dichloromethane
20 was effected. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl

acetate/n-hexane = 1/4) gave the end compound in 131 mg (yield, 83%).

¹H-NMR(270MHz, CDCl₃)δ: 0.77(3H, s), 0.84(3H, s), 0.92-2.20(23H, m), 3.35(3H, s), 3.53(1H, t, J=8.3Hz), 3.92(4H, s), 4.62(2H, d, J=1.8Hz), 4.92-5.04(2H, m), 5.62-5.80(1H, m).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.50

(Step 4)



10

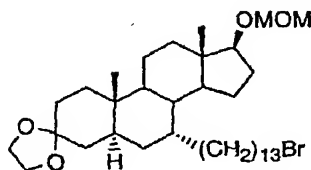
Synthesis of 3,3-ethylenedioxy-17β-methoxymethoxy-7α-(13-bromo-2-tridecen-1-yl)-5α-androstane

3,3-Ethylenedioxy-17β-methoxymethoxy-7α-(2-propen-1-yl)-5α-androstane (42.6 mg) was dissolved in dichloromethane (1.5 ml) and, after adding 12-bromododecene (50.4 mg) and benzylidenebis(tricyclohexylphosphine)-dichlororuthenium (8.4 mg), the mixture was heated under reflux for 5 hours in an argon atmosphere. After standing to cool, purification was performed by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/10) to give the end compound in 56.0 mg (yield, 86%).

¹H-NMR(270MHz, CDCl₃)δ: 0.76(3H, s), 0.83(3H, s), 0.94-

2.14(41H, m), 3.34(3H, s), 3.41(2H, t, J=6.9Hz), 3.52(1H, t, J=8.3Hz), 3.92(4H, s), 4.62(2H, d, J=1.8Hz), 5.22-5.46(2H, m).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.56
(Step 5)

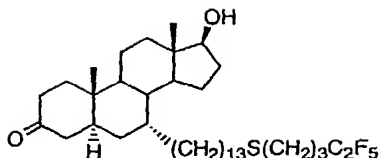


Synthesis of 3,3-ethylenedioxy-17β-methoxymethoxy-7α-(13-bromotridecyl)-5α-androstane

3,3-Ethylenedioxy-17β-methoxymethoxy-7α-(13-bromo-2-tridecen-1-yl)-5α-androstane (55.3 mg) was dissolved in ethyl acetate (2 ml) and, after adding 10%-palladium/carbon (10 mg), the mixture was stirred for 13 hours at 25 °C in a hydrogen atmosphere. After filtering the reaction mixture, the solvent was distilled off at reduced pressure to give the end compound in 47.4 mg (86%).

¹H-NMR(270MHz, CDCl₃)δ: 0.76(3H, s), 0.84(3H, s), 0.94-2.10(45H, m), 3.34(3H, s), 3.41(2H, t, J=6.9Hz), 3.53(1H, t, J=8.3Hz), 3.93(4H, s), 4.62(2H, d, J=1.8Hz).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.56
(Step 6)



Synthesis of 17β-hydroxy-7α-{13-(4,4,5,5,5-pentafluoro-
pentylsulfanyl)tridecyl}-5α-androstan-3-one

5 4,4,5,5,5-Pentafluoropentanethioacetate (35.0 mg) was dissolved in methanol (1 ml) and then 1 M sodium methylate/methanol solution (0.12 ml) was added dropwise. After stirring for 30 minutes, a solution of 3,3-ethylenedioxy-17β-methoxymethoxy-7α-(13-bromotridecyl)-5α-
 10 androstane (47.4 mg) in tetrahydrofuran (1 ml) was added to the reaction mixture. After stirring for 18 hours, water was added to the reaction mixture and extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried
 15 with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Crude purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/10) gave 3,3-ethylenedioxy-17β-methoxymethoxy-7α-{13-(4,4,5,5,5-
 20 pentafluoropentylsulfanyl)-tridecyl}androstane (42.6 mg), which was then dissolved in acetone (2 ml); after adding 2 N-hydrochloric acid (0.5 ml), the mixture was heated under reflux for 3 hours at 60°C. After standing to cool down to 0°C, water was added and extraction with chloroform was
 25 conducted. The organic layer was washed with a saturated

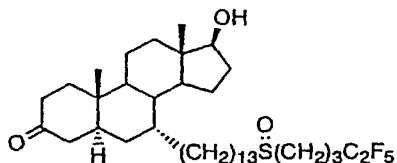
aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/4) gave the end compound in 40.2 mg (82%).

¹H-NMR(270MHz, CDCl₃)δ: 0.76(3H, s), 1.04(3H, s), 0.88-2.40(49H, m), 2.50(2H, t, J=7.3Hz), 2.59(2H, t, J=7.9Hz), 3.58-3.70(1H, m).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.32

(Step 7)

Synthesis of 17β-hydroxy-7α-{13-(4,4,5,5,5-pentafluoropentylsulfinyl)tridecyl}-5α-androstan-3-one



15

17β-Hydroxy-7α-{13-(4,4,5,5,5-pentafluoropentylsulfinyl)tridecyl}-5α-androstan-3-one (26.0 mg) was dissolved in tetrahydrofuran (1 ml) and then OXONE (14.4 mg) and water (0.2 ml) were added at 0°C. After stirring for 30 minutes, a saturated aqueous solution of sodium hydrogencarbonate was added to the reaction mixture and extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after

filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 2/1) gave the end compound in 19.5 mg (73%).

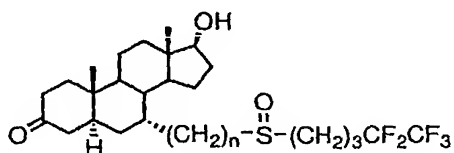
5 $^1\text{H-NMR}$ (270MHz, CDCl_3) δ : 0.76(3H, s), 1.04(3H, s), 0.98-2.40(49H, m), 2.58-2.82(4H, m), 3.60-3.70(1H, m).

Mass(FAB): 681(M+1).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.10

10

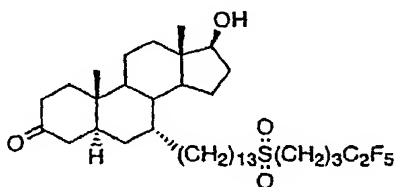
The following compounds were synthesized by similar methods to Example 124.



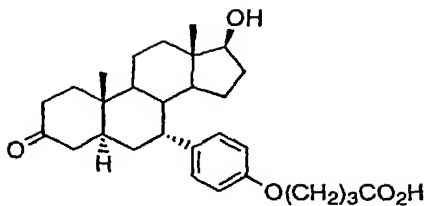
Example	n	MW	Mass (FAB)
125	5	568	569
126	7	596	597
127	9	624	625
128	11	652	653

15 [Example 129]

Synthesis of 17 β -hydroxy-7 α -(13-(4,4,5,5,5-pentafluoropentylsulfonyl)tridecyl)-5 α -androstan-3-one

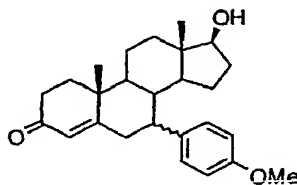


[Example 133]



Synthesis of 17β-hydroxy-7α-(4-(3-carboxypropoxy)phenyl)-5α-androstan-3-one

5 (Step 1)



Synthesis of 17β-hydroxy-7-(4-methoxyphenyl)-5α-androst-4-en-3-one

In an argon atmosphere, copper(I) iodide (1.14 g) was
 10 dissolved in anhydrous tetrahydrofuran (5 ml) and then 0.5
 M 4-methoxyphenylmagnesium bromide/tetrahydrofuran solution
 (11.9 ml) was added dropwise at -50 °C. After stirring
 for 10 minutes, 17β-t-butyldimethylsilyloxyandrost-4,6-
 dien-3-one (600 mg), chlorotrimethylsilane (0.376 ml) and a
 15 tetrahydrofuran solution (6 ml) of hexamethylphosphoric
 triamide (0.518 ml) were added dropwise at -78°C. The
 temperature of the mixture was elevated to -40°C over 1
 hour. To the reaction mixture, 2 N-hydrochloric acid was
 added and, after stirring for 1 hour at 25°C, extraction
 20 with ethyl acetate was conducted. The organic layer was

dried with magnesium sulfate and, after filtering, the solvent was distilled off at reduced pressure.

Purification by silica gel column chromatography

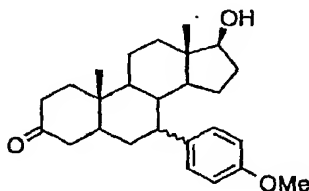
(developing solvents: ethyl acetate/n-hexane = 1/2) gave

5 the end compound in 67.9 mg (yield, 12%) as a diastereomeric mixture.

¹H-NMR(270MHz, CDCl₃)δ: 0.55-0.99(4/3H, m), 0.76(2H, s),
0.81(1H, s), 1.00-2.54(47/3H, m), 1.32(2H, s), 1.34(1H, s),
2.82-3.00(2/3H, m), 3.00-3.08(1/3H, m), 3.40-3.56(1H, m),
10 3.78(1H, s), 3.80(2H, s), 5.71(1H, s), 6.74-6.86(2H, m),
7.04-7.18(2H, m).

R_f value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/1): 0.38

(Step 2)



15

Synthesis of 17β-hydroxy-7-(4-methoxyphenyl)-5α-androstan-3-one

Metallic lithium (11.9 mg) was added to liquid ammonia (15 ml) at -78°C. After stirring for 5 minutes, 17β-
20 hydroxy-7-(4-methoxyphenyl)-5α-androst-4-en-3-one (67.8 mg) and a solution of t-butanol (25.3 μl) in tetrahydrofuran (3 ml) were added and the mixture was stirred for 5 minutes. After adding 1,2-dibromoethane (0.1 ml) and ammonium chloride (1 g), the mixture was stirred

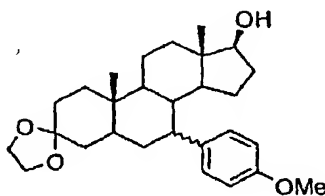
for 30 minutes at 25°C. After adding water, extraction with ethyl acetate was conducted. The organic layer was dried with magnesium sulfate and, after filtering, the solvent was distilled off at reduced pressure.

- 5 Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/2) gave the end compound in 49.8 mg (yield, 73%) as a diastereomeric mixture.

1H-NMR(270MHz, CDCl₃)δ: 0.50-0.62(2/3H, m), 0.73(2H, s),
 10 0.78(1H, s), 0.84-1.00(2/3H, m), 1.11(1H, m), 1.15(2H, m),
 1.04-2.44(58/3H, m), 2.90-3.00(1/3H, m), 3.42-3.58(1H, m),
 3.78(2H, s), 3.79(1H, s), 6.70-7.30(4H, m).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/1): 0.48

- 15 (Step 3)



Synthesis of 3,3-ethylenedioxy-17β-hydroxy-7-(4-methoxyphenyl)-5α-androstane

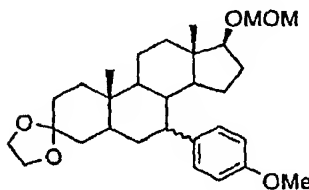
- 17β-Hydroxy-7-(4-methoxyphenyl)-5α-androstan-3-one
 20 (49.7 mg) was dissolved in benzene (2 ml) and, after adding ethylene glycol (0.5 ml) and p-toluenesulfonic acid (2.2 mg), the mixture was heated under reflux as water was continuously removed by means of a Dean-Stark trap. After one hour, the reaction mixture was cooled to 0°C and, after

adding a saturated aqueous solution of sodium hydrogencarbonate, extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure to give the end compound in 55.0 mg (yield, 100%) as a diastereomeric mixture.

¹H-NMR(270MHz, CDCl₃)δ: 0.54-0.60(2/3H, m), 0.70(2H, s), 0.75(1H, s), 0.91(1H, s), 0.95(2H, s), 0.90-1.98(58/3H, m), 2.22-2.38(2/3H, m), 2.86-2.94(1/3H, m), 3.44-3.58(1H, m), 3.72-3.98(4H, m), 3.78(2H, s), 3.80(1H, s), 6.70-7.30(4H, m).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/1): 0.52

(Step 4)



Synthesis of 3,3-ethylenedioxy-17β-methoxymethoxy-7-(4-methoxyphenyl)-5α-androstane

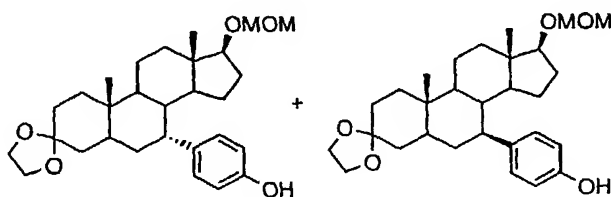
To a solution of 3,3-ethylenedioxy-17β-hydroxy-7-(4-methoxyphenyl)-5α-androstane (55.0 mg) in dichloromethane (2 ml), diisopropylethylamine (0.128 ml) and chloromethyl methyl ether (0.047 ml) were added dropwise at 0°C. After stirring for 12 hours at 25°C, a saturated aqueous solution of sodium hydrogencarbonate was added to the reaction

mixture and extraction with dichloromethane was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at
 5 reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/4) gave the end compound in 56.2 mg (yield, 93%) as a diastereomeric mixture.

¹H-NMR(270MHz, CDCl₃)δ: 0.42-0.60(2/3H, m), 0.74(2H, s),
 10 0.78(1H, s), 0.80-0.90(2/3H, m), 0.91(1H, s), 0.94(2H, s),
 1.00-1.96(56/3H, m), 2.22-2.36(2/3H, m), 2.84-2.92(1/3H, m),
 3.30(3H, s), 3.34-3.44(1H, m), 3.78(2H, s), 3.80(1H, s),
 3.82-3.98(4H, m), 4.56(2H, s), 6.70-7.30(4H, m).

R_f value (on silica gel plate, developing solvents: ethyl
 15 acetate/n-hexane = 1/1): 0.68

(Step 5)



Synthesis of 3,3-ethylenedioxy-17β-methoxymethoxy-7α-(4-hydroxyphenyl)-5α-androstane and 3,3-ethylenedioxy-17β-methoxymethoxy-7β-(4-hydroxyphenyl)-5α-androstane
 20

To a solution of 3,3-ethylenedioxy-17β-methoxymethoxy-7-(4-methoxyphenyl)-5α-androstane (151 mg) in N,N-dimethylacetamide (3 ml), sodium thiomethylate (109 mg) was added and the mixture was heated under reflux. After 3

hours, the reaction mixture was cooled to 0°C and, after adding water, extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium

5 sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/4) gave the end compound as both 7 α form in 42.3 mg (yield, 29%) and 7 β form in 88.0 mg (yield, 60%).

10 3,3-ethylenedioxy-17 β -methoxymethoxy-7 α -(4-hydroxyphenyl)-
5 α -androsterane:

¹H-NMR(270MHZ, CDCl₃)δ: 0.78(3H, s), 0.90(3H, s), 1.00-2.08(20H, m), 2.84-2.92(1H, m), 3.30(3H, s), 3.38(1H, t, J=8.6Hz), 3.80-3.94(4H, m), 4.56(2H, s), 4.64(1H, s),

15 6.72(2H, d, J=8.4Hz), 7.23(2H, d, J=8.4Hz).

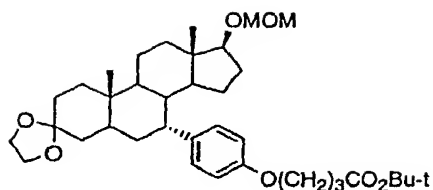
Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.20

3,3-ethylenedioxy-17 β -methoxymethoxy-7 β -(4-hydroxyphenyl)-
5 α -androstande:

20 1H-NMR(270MHz, CDCl₃)δ: 0.46-0.60(1H, m), 0.73(3H, s),
0.94(3H, s), 0.82-1.96(19H, m), 2.22-2.34(1H, m), 3.30(3H,
s), 3.38(1H, t, J=8.6Hz), 3.93(4H, brs), 4.56(2H, s),
4.68(1H, s), 6.66(1H, dd, J=2.3, 8.2Hz), 6.74(1H, dd, J=2.3,
8.2Hz), 6.92(1H, dd, J=1.8, 8.2Hz), 7.07(1H, dd, J=1.8,
25 8.2Hz).

Rf value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.28

(Step 6)



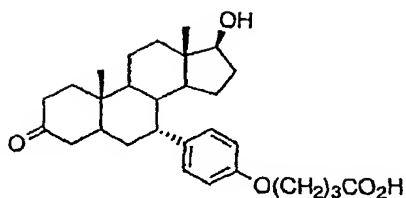
Synthesis of 3,3-ethylenedioxy-17β-methoxymethoxy-7α-(4-(3-t-butoxycarboxypropoxy)phenyl)-5α-androstane

5 To an N,N-dimethylacetamide solution (0.5 ml) of 3,3-ethylenedioxy-17β-methoxymethoxy-7α-(4-hydroxyphenyl)-5α-androstane (22.0 mg), t-butyl 4-bromobutyrate (31.3 mg), potassium carbonate (64.5 mg) and 18-crown-6 (123 mg) were added. After one hour, water was added to the reaction
10 mixture and extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column
15 chromatography (developing solvents: ethyl acetate/n-hexane = 1/8) gave the end compound in 27.8 mg (yield, 99%).

¹H-NMR(270MHz, CDCl₃)δ: 0.78(3H, s), 0.90(3H, s), 1.04-2.12(22H, m), 1.46(9H, s), 2.43(2H, t, J=7.3Hz), 2.82-2.92(1H, m), 3.30(3H, s), 3.38(1H, t, J=8.4Hz), 3.80-
20 3.94(4H, m), 3.97(2H, t, J=6.1Hz), 4.56(2H, s), 6.78(2H, d, J=8.6Hz), 7.26(2H, d, J=8.6Hz).

R_f value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/4): 0.40

(Step 7)



Synthesis of 17β-hydroxy-7α-[4-(3-carboxypropoxy)phenyl]-5α-androstan-3-one

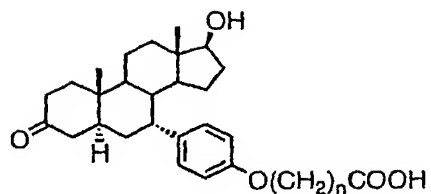
5 3,3-Ethylenedioxy-17β-methoxymethoxy-7α-(4-(3-methoxycarbonylpropoxy)phenyl)-5α-androstane (27.6 mg) was dissolved in acetone (2 ml) and, after adding 2 N-hydrochloric acid (0.5 ml), the mixture was heated at 60°C. After two hours, water was added to the reaction mixture, and extraction with dichloromethane was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: dichloromethane/methanol = 10/1) gave the end compound in 19.2 mg (yield, 89%).

1H-NMR(270MHz, CDCl₃)δ: 0.78(3H, s), 1.10(3H, s), 1.00-2.44(22H, m), 2.60(2H, t, J=7.3Hz), 2.88-2.96(1H, m), 3.50(1H, t, J=8.2Hz), 4.00(2H, t, J=5.9Hz), 6.77(2H, d, J=8.6Hz), 7.20(2H, d, J=8.6Hz).

Mass (FAB): 469(M+1).

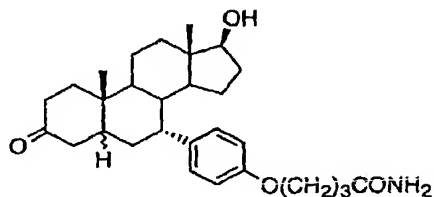
Rf value (on silica gel plate, developing solvent: ethyl acetate): 0.54

The following compounds were synthesized by similar methods to Example 133.



Example	n	MW	Mass (FAB)
134	1	440	441
135	7	524	525

[Example 136]



5

Synthesis of 17β-hydroxy-7α-{4-(3-carbamoylpropoxy)phenyl}-5α-androstan-3-one

The 17β-hydroxy-7α-{4-(3-carboxypropoxy)phenyl}-5α-androstan-3-one obtained in Example 133 was dissolved in tetrahydrofuran (0.5 ml) and then triethylamine (3.2 μl) and ethyl chloroformate (1.8 μl) were added dropwise under cooling with ice. After stirring for 5 minutes, ammonia gas was bubbled for 1 minute. After stirring for 15 minutes, water was added to the reaction mixture and extraction with dichloromethane was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced

pressure. Purification by preparative chromatography (developing solvents: dichloromethane/methanol = 20/1) gave the end compound in 6.6 mg (yield, 90%).

¹H-NMR(270MHz, CDCl₃)δ: 0.78(3H, s), 1.11(3H, s), 1.00-2.44(22H, m), 2.45(2H, t, J=7.1Hz), 2.88-2.98(1H, m), 3.50(1H, t, J=8.2Hz), 4.01(2H, t, J=5.7Hz), 5.30-5.60(2H, m), 6.77(2H, d, J=8.6Hz), 7.20(2H, d, J=8.6Hz).

Mass (FAB): 468(M+1).

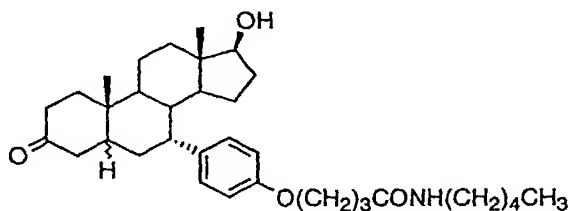
Rf value (on silica gel plate, developing solvents: dichloromethane/methanol = 20/1): 0.14

The following compounds were synthesized by similar methods to Example 136.



Example	n	MW	Mass (FAB)
137	1	439	440
138	7	523	524

15 [Example 139]



Synthesis of 17β-hydroxy-7α-4-{3-(N-pentylcarbamoyl)propoxy}phenyl)-5α-androstan-3-one

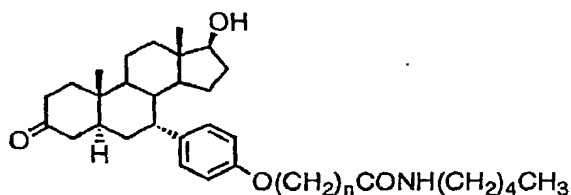
The 17 β -hydroxy-7 α -{4-(3-carboxypropoxy)phenyl}-5 α -androstan-3-one (7.0 mg) obtained in Example 133 was dissolved in tetrahydrofuran (0.5 ml) and then 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (8.6 mg), 1-hydroxybenzotriazole monohydrate (6.8 mg) and pentylamine (10.4 ml) were added at 25°C. After stirring for 4 hours, a saturated aqueous solution of sodium hydrogencarbonate was added to the reaction mixture and extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by preparative chromatography (developing solvent: ethyl acetate) gave the end compound in 5.8 mg (yield, 72%).

¹H-NMR(270MHz, CDCl₃) δ : 0.78(3H, s), 0.80-0.94(3H, m), 1.11(3H, s), 1.00-2.44(30H, m), 2.88-2.98(1H, m), 3.24(2H, dt, J=6.1, 7.1Hz), 3.50(1H, t, J=8.3Hz), 3.99(2H, t, J=5.8Hz), 5.50(1H, brs), 6.77(2H, d, J=8.6Hz), 7.20(2H, d, J=8.6Hz).

Mass (FAB): 538(M+1).

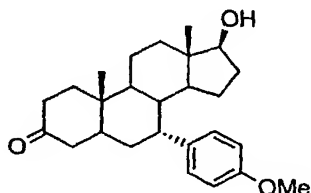
R_f value (on silica gel plate, developing solvent: ethyl acetate): 0.62

The following compound was synthesized by a similar method to Example 139.



Example	n	MW	Mass (FAB)
140	7	593	594

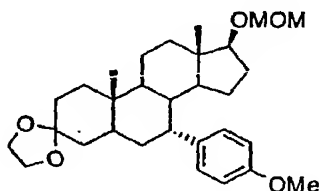
[Example 141]



Synthesis of 17β-hydroxy-7α-(4-methoxyphenyl)-5α-androstan-

5 3-one

(Step 1)



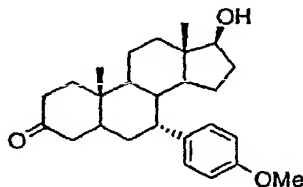
Synthesis of 3,3-ethylenedioxy-17β-methoxymethoxy-7α-(4-
methoxyphenyl)-5α-androstane

10 The 3,3-ethylenedioxy-17β-methoxymethoxy-7α-(4-
hydroxyphenyl)-5α-androstane (10.0 mg) obtained in step 5
of Example 136 was dissolved in N,N-dimethylformamide (1
ml) and then 60% sodium hydride (2.5 mg) and iodomethane
(13.2 μl) were added at 0°C. After stirring for 13 hours
15 at 25°C, a saturated aqueous solution of NH₄Cl was added to
the reaction mixture and extraction with ethyl acetate was
conducted. The organic layer was washed with a saturated
aqueous solution of sodium chloride and dried with
magnesium sulfate; after filtering, the solvent was

distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/4) gave the end compound in 10.2 mg (yield, 99%).

5 $^1\text{H-NMR}$ (270MHz, CDCl_3) δ : 0.78(3H, s), 0.91(3H, s), 1.00-1.96(20H, m), 2.84-2.92(1H, m), 3.30(3H, s), 3.38(1H, t, $J=8.6\text{Hz}$), 3.80(3H, s), 3.82-3.92(4H, m), 4.56(2H, s), 6.80(2H, d, $J=8.6\text{Hz}$), 7.27(2H, d, $J=8.6\text{Hz}$).

R_f value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1:1): 0.68
10 (Step 2)



Synthesis of 17β-hydroxy-7α-(4-methoxyphenyl)androstane-3-one

15 3,3-Ethylenedioxy-17β-methoxymethoxy-7α-(4-methoxyphenyl)androstane (10.2 mg) was dissolved in acetone (2 ml) and, after adding 2 N-hydrochloric acid (0.5 ml), the mixture was heated under reflux. After 2 hours, water was added to the reaction mixture and extraction with
20 dichloromethane was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography

(developing solvents: ethyl acetate/n-hexane = 1/1) gave the end compound in 7.2 mg (yield, 85%).

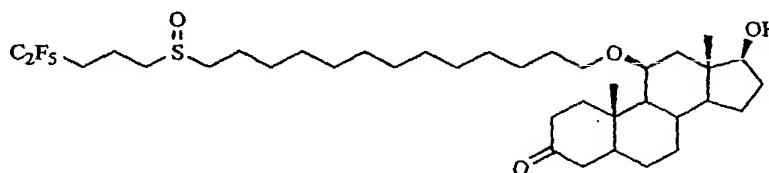
¹H-NMR(270MHz, CDCl₃)δ: 0.78(3H, s), 1.11(3H, s), 1.00-2.50(20H, m), 2.88-2.96(1H, m), 3.50(1H, t, J=8.6Hz),
5 3.79(3H, s), 6.79(2H, d, J=8.7Hz), 7.22(2H, d, J=8.7Hz).

Mass (FAB): 397(M+1).

R_f value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 1/1): 0.48

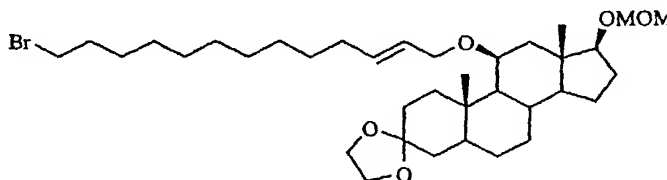
[Example 142]

10 Synthesis of 17β-hydroxy-11β-(13-(4,4,5,5,5-pentafluoropentylsulfinyl)tridecyloxy)-5α-androstan-3-one



(Step 1)

15 3,3-ethylenedioxy-17β-methoxymethoxy-11β-(13-bromo-2-tridecenylloxy)-5α-androstane



In an argon atmosphere, the 3,3-ethylenedioxy-17β-(methoxymethoxy)-11β-(2-propen-1-yloxy)-5α-androstane (100.8 mg) obtained in step 2 of Example 104, 12-bromododecan-1-ene (114.7 mg) and,
20

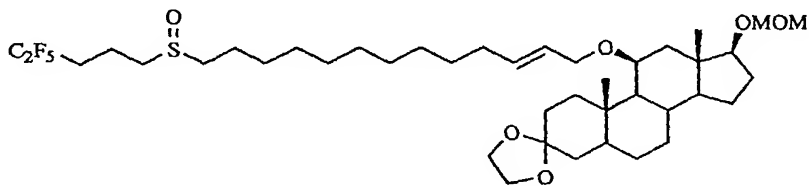
5

¹H-NMR(270MHz, CDCl₃)δ: 0.95(3H, s), 1.02(3H, s), 0.69-2.38(42H, m), 2.50(2H, t, J=7.3Hz), 2.59(2H, t, J=6.9Hz), 3.36(3H, s), 3.47(1H, t, J=8.2Hz), 3.59-4.17(3H, m).

10

Rf value (on silica gel plate, developing solvents: ethyl acetate/hexane = 1/4): 0.42

(Step 3)

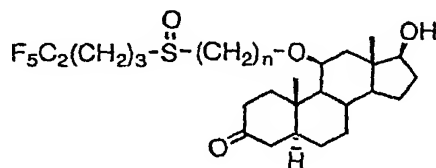


adding 1 N-hydrochloric acid (1 ml), the mixture was heated under reflux for 3 hours. After standing to cool, a saturated aqueous solution of sodium hydrogencarbonate was added to the reaction mixture and extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 2/1) gave the end compound in 20.5 mg (yield, 78%).

¹H-NMR(270MHz, CDCl₃)δ: 0.94(3H, s), 1.24(3H, s), 0.68-2.54(47H, m), 2.58-2.83(4H, m), 3.04-3.16(1H, m), 3.51-3.63(2H, m), 3.72-3.79(1H, m).

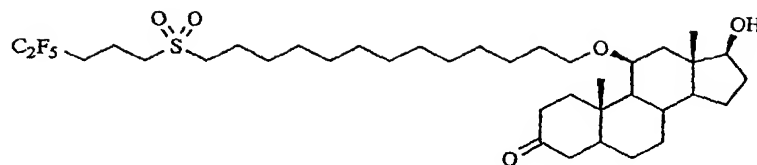
Mass (FAB): 697(M+1).

The following compounds were synthesized by similar methods to Example 142.



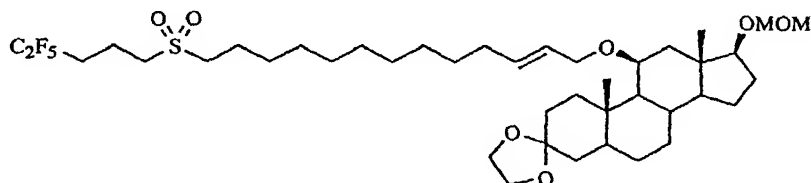
Example	n	MW	Mass (FAB)
143	5	584	585
144	7	612	613
145	9	640	641
146	11	668	669

[Example 147]



Synthesis of 17β-hydroxy-11β-{13-(4,4,5,5,5-pentafluoropentylsulfonyl)tridecyloxy}-5α-androstan-3-one

5 (Step 1)



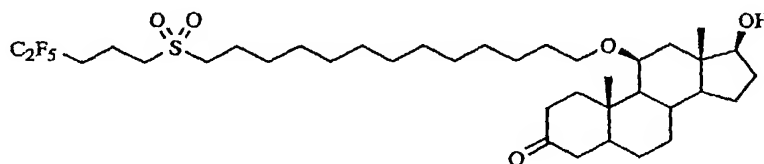
3,3-ethylenedioxy-17β-methoxymethoxy-11β-{13-(4,4,5,5,5-pentafluoropentylsulfonyl)-2-tridecenyloxy}-5α-androstane

3,3-Ethylenedioxy-17β-methoxymethoxy-11β-{13-
 10 (4,4,5,5,5-pentafluoropentylthio)-2-tridecenyloxy}-5α-androstane (47.2 mg) was dissolved in tetrahydrofuran (0.6 ml) and, after adding OXONE (75.7 mg) and water (0.3 ml) at room temperature, the mixture was stirred for 1 hour. After adding a saturated aqueous solution of sodium
 15 hydrogencarbonate to the reaction mixture, extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; then, the solvent was distilled off at reduced pressure. Purification by silica
 20 gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/3) gave the end compound in 33.6 mg

... ..

5 5.37-5.70 (2H, m).

(Step 2)



10 17 β -hydroxy-11 β -{13-(4,4,5,5,5-
pentafluoropentylsulfonyl)tridecyloxy}-5 α -androstan-3-one
3,3-Ethylenedioxy-17 β -methoxymethoxy-11 β -{13-
(4,4,5,5,5-pentafluoropentylsulfonyl)-2-tridecenyloxy}-5 α -
androstane (33.6 mg) was dissolved in ethyl acetate (1 ml)
15 and, after adding 10% palladium/carbon (10 mg), the mixture
was stirred for 4 hours at room temperature in a hydrogen
atmosphere. After filtering the reaction mixture, the
solvent was distilled off at reduced pressure and the
resulting residue was dissolved in acetone (2 ml); after
20 adding 1 N-hydrochloric acid (1 ml), the mixture was heated
under reflux for 4 hours. After standing to cool, a
saturated aqueous solution of sodium hydrogencarbonate was
added and extraction with ethyl acetate was effected. The
organic layer was washed with a saturated aqueous solution

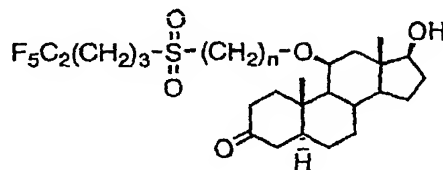
of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 2/3) gave the end compound in 22.9 mg (yield, 76%).

$^1\text{H-NMR}$ (270MHz, CDCl_3) δ : 0.94(3H, s), 1.24(3H, s), 0.68-2.54(47H, m), 2.92-3.15(5H, m), 3.51-3.64(2H, m), 3.72-3.78(1H, m).

Mass (FAB): 713(M+1).

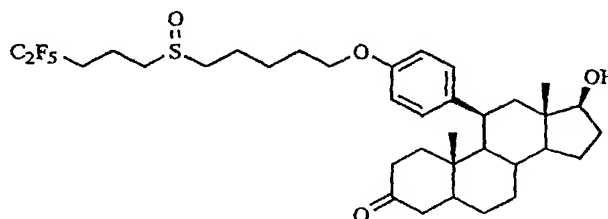
10

The following compounds were synthesized by similar methods to Example 147.



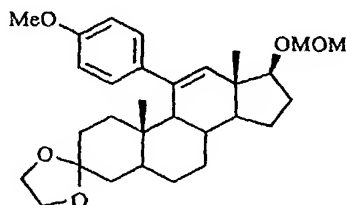
Example	n	MW	Mass (FAB)
148	7	628	629
149	9	656	657
150	11	684	685

15 [Example 151]



17 β -hydroxy-11 β -[4-{5-(4,4,5,5,5-pentafluoropentylsulfinyl)pentyl}oxy]phenyl]-5 α -androstan-3-one

(Step 1)



5

3,3-ethylenedioxy-17 β -methoxymethoxy-11-(4-methoxyphenyl)-5 α -androst-11-ene

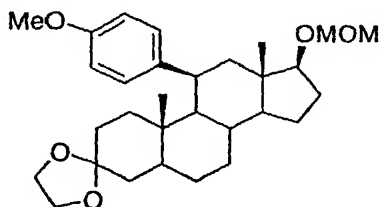
A mixture of 3,3-ethylenedioxy-17 β -methoxymethoxy-11-
 [{1,1,2,2,3,3,4,4,4-nonafluorobutyl)sulfonyl}oxy]-5 α -
 10 androst-11-ene (98.8 mg), 4-methoxyphenylboronic acid (223
 mg), tetrakis(triphenylphosphine) palladium (6.8 mg), lithium
 chloride (12.4 mg), 2 M aqueous solution of sodium
 carbonate (0.5 ml), toluene (2 ml) and ethanol (1 ml) was
 heated under reflux for 13 hours in an argon atmosphere.
 15 After adding a saturated aqueous solution of sodium
 hydrogencarbonate to the reaction mixture, extraction with
 ethyl acetate was conducted. The organic layer was washed
 with a saturated aqueous solution of sodium chloride and
 dried with magnesium sulfate; after filtering, the solvent
 20 was distilled off at reduced pressure. Purification by
 silica gel column chromatography (developing solvents:
 ethyl acetate/n-hexane = 1/6) gave the end compound in 65.4
 mg (yield, 93%).

¹H-NMR(270MHz, CDCl₃) δ : 0.59-2.28(18H, m), 0.85(3H, s),

0.94(3H, s), 3.31(3H, s), 3.63(1H, t, J=8.0Hz), 3.78(3H, s),
3.80-3.96(4H, m), 4.57(1H, d, J=6.6Hz), 4.61(1H, d,
J=6.6Hz), 5.86(1H, d, J=1.7Hz), 6.68-6.83(2H, m), 6.95-
7.08(2H, m).

5 Rf value (on silica gel plate, developing solvents: ethyl
acetate/hexane = 1/4): 0.40

(Step 2)



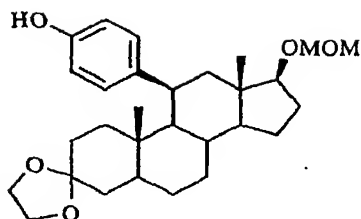
10 3,3-ethylenedioxy-17β-methoxymethoxy-11β-(4-methoxyphenyl)-
5α-androstane

3,3-Ethylenedioxy-17β-methoxymethoxy-11-(4-
methoxyphenyl)-5α-androst-11-ene (29.9 mg) was dissolved in
ethyl acetate (2 ml) and, after adding acetic acid (0.2 ml)
and 10%-palladium/carbon (30 mg), the mixture was stirred
15 for 3 hours at 25°C under hydrogen pressure (25 atm).
After filtering the reaction mixture, the solvent was
distilled off at reduced pressure and the reaction mixture
was purified by silica gel column chromatography
(developing solvents: ethyl acetate/dichloromethane =
20 1/20) to give the end compound in 20.1 mg (yield, 67%).

¹H-NMR(300MHz, CDCl₃)δ: 7.40-7.25(2H, m), 6.75(2H, d,
J=8.2Hz), 4.55(3H, s), 3.92(4H, s), 3.78(3H, s), 3.42(1H,
dd, J=6.8, 6.6Hz), 3.38-3.28(1H, m), 3.28(3H, s), 2.40-
0.80(20H, m), 0.76(3H, s), 0.65(3H, s).

Mass (EI): 484(M+).

(Step 3)



3,3-ethylenedioxy-17β-methoxymethoxy-11β-(4-hydroxyphenyl)-

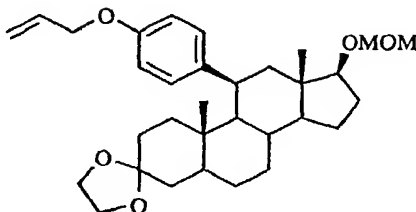
5 5α-androstane

3,3-Ethylenedioxy-17β-methoxymethoxy-11β-(4-methoxyphenyl)-5α-androstane (114.8 mg) and a solution of sodium methanethiolate (69.9 mg) in dimethylformamide (3 mm1) were heated under reflux for 1 hour in a nitrogen atmosphere. After standing to cool, a saturated aqueous solution of ammonium chloride was added to the reaction mixture and extraction with ethyl acetate was effected. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/2) gave the end compound in 105.2 mg (yield, 94%).

20 ¹H-NMR(270MHz, CDCl₃)δ: 0.65(3H, s), 0.75(3H, s), 0.90-2.19(20H, m), 3.28(3H, s), 3.24-3.34(1H, m), 3.43(1H, t, J=8.1Hz), 3.91(4H, s), 4.54(2H, s), 4.64(1H, s), 6.64(2H, d, J=8.7Hz), 7.13-7.32(2H, m).

Rf value (on silica gel plate, developing solvents: ethyl acetate/hexane = 1/2): 0.29

(Step 4)



5 3,3-ethylenedioxy-17β-methoxymethoxy-11β-(4-(2-propen-1-yloxy)phenyl)-5α-androstane

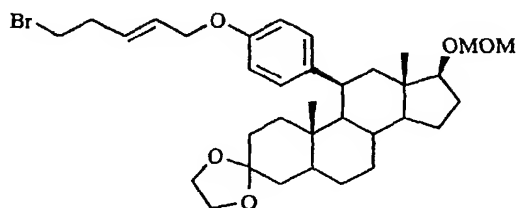
To a solution of 3,3-ethylenedioxy-17β-methoxymethoxy-11β-(4-hydroxyphenyl)-5α-androstane (56.2 mg) in dimethylformamide (2 ml), sodium hydride (9.6 mg) was added under cooling with ice and the mixture was stirred for 5 minutes. After adding allyl bromide (28.9 mg), the mixture was stirred for 1 hour under cooling with ice. After adding water to the reaction mixture, extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/2) gave the end compound in 51.0 mg (yield, 84%).

¹H-NMR(270MHz, CDCl₃)δ: 0.65(3H, s), 0.76(3H, s), 0.82-2.18(20H, m), 3.28(3H, s), 3.24-3.36(1H, m), 3.43(1H, t, J=8.0Hz), 3.90(4H, s), 4.49(2H, d, J=5.3Hz), 4.53(2H, s), 5.26(1H, dd, J=10.5, 1.2Hz), 5.40(1H, dd, J=17.3, 1.5Hz),

5.98-6.13(1H, m), 6.72(2H, d, J=8.7Hz), 7.26(2H, brs).

Rf value (on silica gel plate, developing solvents: ethyl acetate/hexane = 1/2): 0.59

(Step 5)



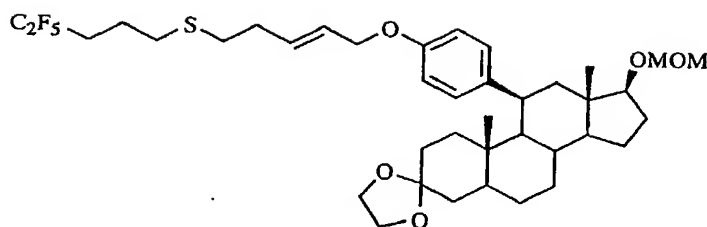
3,3-ethylenedioxy-17β-methoxymethoxy-11β-{4-(5-bromo-2-penten-1-yloxy)phenyl}-5α-androstane

In an argon atmosphere, 3,3-ethylenedioxy-17β-methoxymethoxy-11β-(4-(2-propen-1-yloxy)phenyl)-5α-androstane (16.0 mg), 4-bromo-1-butene (8.5 mg) and benzyldienebistricyclohexylphosphine dichlororuthenium (2.6 mg) were dissolved in dichloromethane (0.3 ml) and the mixture was stirred for 16.5 hours at room temperature. The solvent was distilled off at reduced pressure and purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/4) gave the end compound in 14.4 mg (yield, 74%).

¹H-NMR(270MHz, CDCl₃)δ: 0.65(3H, s), 0.76(3H, s), 0.81-2.18(20H, m), 2.60-2.78(2H, m), 3.28(3H, s), 3.41(2H, t, J=6.9Hz), 3.25-3.34(1H, m), 3.37-3.48(1H, m), 3.90(4H, s), 4.43-4.51(2H, m), 4.54(2H, s), 5.77-5.88(2H, m), 6.71(2H, d, J=8.7Hz), 7.26(2H, brs).

Rf value (on silica gel plate, developing solvents: ethyl acetate/hexane = 1/4): 0.48

$\frac{d}{dt} \left(\frac{\partial L}{\partial \dot{x}} \right) = \frac{\partial L}{\partial x}$



5 androstane

10 solution) (0.05 ml) were dissolved in methanol (0.2 ml) and
tetrahydrofuran (0.2 ml) and the solution was stirred for
17 hours at room temperature. After adding water to the
reaction mixture, extraction with ethyl acetate was
conducted. The organic layer was washed with a saturated
15 aqueous solution of sodium chloride and dried with
magnesium sulfate; then, the solvent was distilled off at
reduced pressure. Purification by silica gel column
chromatography (developing solvents: ethyl acetate/n-
hexane = 1/4) gave the end compound in 14.8 mg (yield, 87%).

20 ¹H-NMR(270MHz, CDCl₃)δ: 0.65(3H, s), 0.75(3H, s), 0.81-
2.49(26H, m), 2.54-2.67(4H, m), 3.28(3H, s), 3.43(1H, t,
J=7.9Hz), 3.24-3.37(1H, m), 3.90(4H, s), 4.45(2H, d,
J=4.8Hz), 4.53(2H, s), 5.66-5.94(2H, m), 6.71(2H, d,

[illegible]

Chemical structure of compound 10: A steroid derivative. It features a C₂F₅ group attached to a sulfonamide group (SO₂NH-) which is linked to a chain containing a double bond and an ether linkage (-O-). This chain is further connected to a phenyl ring. The steroid core has a 3,4-epoxide and an OMOM group at the 17-position.

5

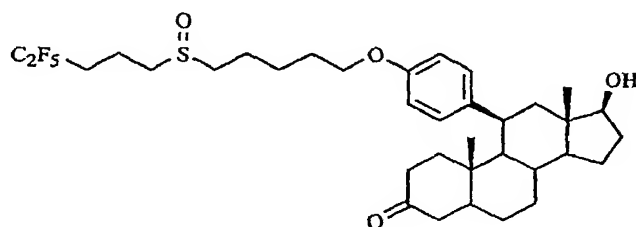
10

15

2.37(24H, m), 2.55-2.90(6H, m), 3.28(3H, s), 3.43(1H, t, J=7.8Hz), 3.24-3.37(1H, m), 3.90(4H, s), 4.38-4.51(2H, m), 4.53(2H, s), 5.68-5.95(2H, m), 6.71(2H, d, J=8.6Hz), 7.26(2H, brs).

5 Rf value (on silica gel plate, developing solvents: ethyl acetate/hexane = 1/2): 0.07

(Step 8)



10 17β-hydroxy-11β-[4-{5-(4,4,5,5,5-pentafluoropentylsulfinyl)pentenyloxy}phenyl]-5α-androstan-3-one

3,3-Ethylenedioxy-17β-methoxymethoxy-11β-[4-{5-(4,4,5,5,5-pentafluoropentylsulfinyl)-2-pentenyloxy}phenyl]-5α-androstane (14.2 mg) was dissolved
15 in ethyl acetate (1 ml) and, after adding 10% palladium/carbon (10 mg), the mixture was stirred for 2 hours at room temperature in a hydrogen atmosphere. After filtering the reaction mixture, the solvent was distilled off at reduced pressure and the resulting residue was
20 dissolved in acetone (2 ml); after adding 1 N-hydrochloric acid (1 ml), the reaction mixture was heated under reflux for 1.5 hours. After standing to cool, a saturated aqueous solution of sodium hydrogencarbonate was added and

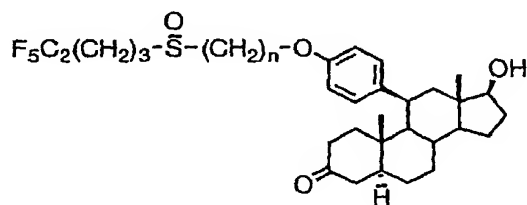
extraction with ethyl acetate was effected. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced

5 pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 4/1) gave the end compound in 11.5 mg (yield, 92%).

¹H-NMR(270MHz, CDCl₃)δ: 0.75(3H, s), 0.86(3H, s), 0.82-2.37(31H, m), 2.62-2.87(4H, m), 3.28-3.40(1H, m), 3.48-10 3.58(1H, m), 3.96(2H, t, J=6.0Hz), 6.72(2H, d, J=8.7Hz), 7.26(2H, brs).

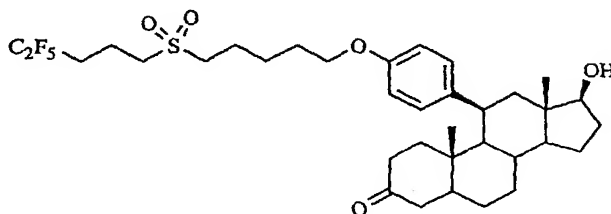
Mass (FAB): 661(M+1).

The following compound was synthesized by a similar
15 method to Example 151.



Example	n	MW	Mass(ESI)
152	7	688	689

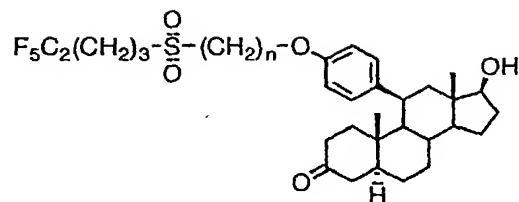
[Example 153]



The 17 β -hydroxy-11 β -[4-{7-(4,4,5,5,5-pentafluoropentylsulfinyl)pentyl}oxy]phenyl]-5 α -androstan-3-one (3.0 mg) obtained in Example 151 was dissolved in tetrahydrofuran (1.0 ml) and, after adding OXONE (2.8 mg) and water (0.5 ml) at room temperature, the mixture was stirred for 1.5 hours. After adding a saturated aqueous solution of sodium hydrogencarbonate to the reaction mixture, extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; then, the solvent was distilled off at reduced pressure.

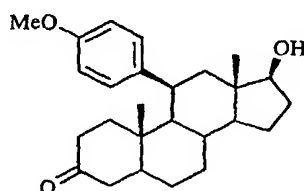
1H-NMR(270MHz, CDCl₃)δ: 0.75(3H, s), 0.86(3H, s), 0.78-2.39(31H, m), 2.98-3.09(4H, m), 3.29-3.38(1H, m), 3.48-3.59(1H, m), 3.96(2H, t, J=5.9Hz), 6.72(2H, d, J=8.4Hz), 7.26(2H, brs).

The following compound was synthesized by a similar method to Example 153.



Example	n	MW	Mass (FAB)
154	7	704	705

[Example 155]



5

Synthesis of 17β-hydroxy-11β-(4-methoxyphenyl)-5α-androstan-3-one

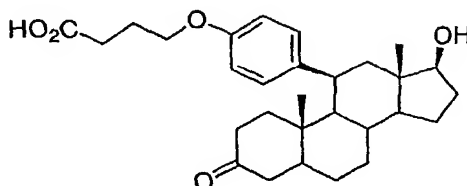
To a solution of 3,3-ethylenedioxy-17β-methoxymethoxy-11β-(4-methoxyphenyl)-5α-androstane (5.8 mg) in acetone (2 ml), 1 N-hydrochloric acid (1 ml) was added and the mixture was heated under reflux for 1 hour. After standing to cool, a saturated aqueous solution of sodium hydrogencarbonate was added and extraction with ethyl acetate was conducted. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried with magnesium sulfate; after filtering, the solvent was distilled off at reduced pressure. Purification by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/1) gave the end compound in 4.6 mg (yield, 97%).

$^1\text{H-NMR}$ (270 MHz, CDCl_3) δ : 0.75 (3H, s), 0.86 (3H, s), 0.82-2.30 (21H, m), 3.31-3.39 (1H, m), 3.48-3.59 (1H, m), 3.79 (3H, s), 6.74 (2H, d, $J=8.7\text{Hz}$), 7.28 (2H, brs).

Mass (EI): 396 (M^+).

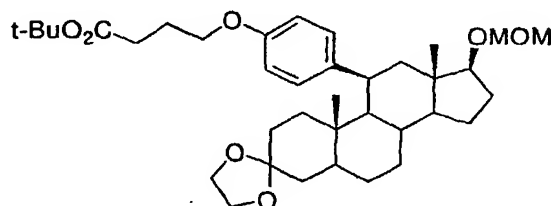
5

[Example 156]



Synthesis of 17β-hydroxy-11β-[4-(3-carboxypropyloxy)phenyl]-5α-androstan-3-one

10 (Step 1)



3,3-ethylenedioxy-17β-methoxymethoxy-11β-[4-(3-tert-butoxycarbonylpropyloxy)phenyl]-5α-androstane

In a nitrogen atmosphere, 3,3-ethylenedioxy-17β-methoxymethoxy-11β-(4-hydroxyphenyl)-5α-androstane (30.2 mg), potassium carbonate (89 mg), 3-bromobutanoic acid t-butyl ester (0.029 ml), potassium iodide (21.3 mg) and 18-crown-6 (200 mg) were dissolved in N,N-dimethylacetamide (0.5 ml) and the mixture was stirred for 10 minutes at 60°C. After adding water to the reaction mixture, extraction was

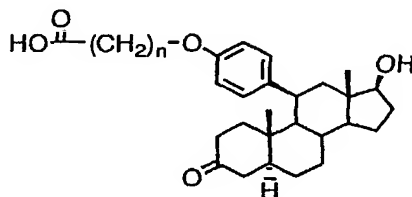
gel column chromatography (developing solvents: ethyl acetate/n-hexane: 1/1) gave the end compound in 29.0 mg (yield, 100%).

1H-NMR(300MHz, CDCl₃)δ: 7.40-7.10(2H, m), 6.72(2H, d, J=8.8Hz), 3.84(1H, brs), 3.99(2H, t, J=6.0Hz), 3.54(1H, dd, J=7.1, 8.5Hz), 3.33(1H, dd, J=5.8, 6.0Hz), 2.57(2H, t, J=7.1Hz), 2.28-1.86(11H, m), 1.74-1.16(9H, m), 1.08-0.90(2H, m), 0.85(3H, s), 0.74(3H, s).

Mass (ESI): 469(M+1).

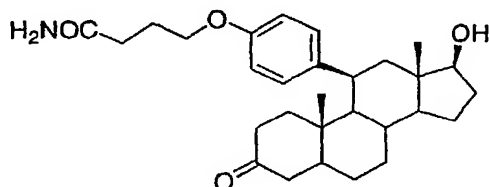
10

The following compound was synthesized by a similar method to Example 156.



Example	n	MW	Mass (FAB)
157	7	524	525

15 [Example 158]



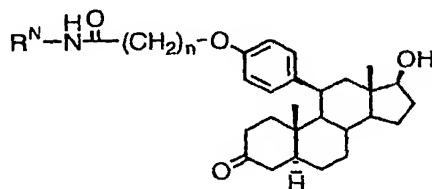
17β-hydroxy-11β-[4-(3-aminocarbonylpropyloxy)phenyl]-5α-androstan-3-one

The 17 β -hydroxy-11 β -[4-(3-carboxypropyloxy)phenyl]-5 α -androstan-3-one (3.6 mg) obtained in Example 156 was dissolved in dichloromethane (0.2 ml) and, after adding triethylamine (5.4 μ l) and ethyl chlorocarbonate (2.2 μ l) at -10°C, the mixture was stirred for 5 minutes. Ammonia gas was blown into the reaction mixture for 5 minutes and the mixture was stirred for 15 minutes at -10°C. After adding a saturated aqueous solution of sodium chloride to the reaction mixture, extraction with dichloromethane and drying with sodium sulfate were effected; after filtering, the solvent was distilled off at reduced pressure. The resulting residue was purified by silica gel column chromatography (developing solvent: ethyl acetate) to give the end compound in 3.6 mg (yield, 100%).

¹H-NMR(300MHz, CDCl₃) δ : 7.40-7.18(2H, m), 6.73(2H, d, J=9.1Hz), 5.48(2H, br), 4.01(2H, t, J=6.0Hz), 3.54(1H, dd, J=7.1, 8.5Hz), 3.34(1H, dd, J=6.0, 6.6Hz), 2.29-1.87(10H, m), 1.78-1.18(10H, m), 1.08-0.90(2H, m), 0.85(3H, s), 0.74(3H, s).

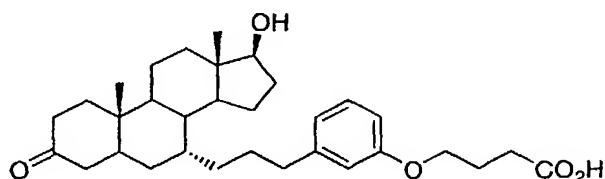
Mass (ESI): 468(M+1).

The following compounds were synthesized by similar methods to Example 158.



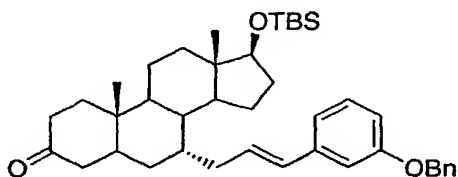
Example	n	R ^N	MW	Mass
159	3	n-pentyl	537	537(EI)
160	7	H	523	524(ESI)
161	7	n-pentyl	593	593(EI)

[Example 162]



Synthesis of 17β-hydroxy-7α-[3-(3-

5 carboxypropyloxyphenyl)propyl]-5α-androstan-3-one
(Step 1)



17β-(t-butyldimethylsilyloxy)-7α-[3-(3-benzyloxy)phenyl]-2-
propenyl]-5α-androstan-3-one

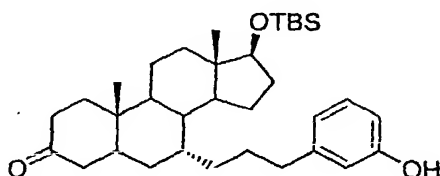
10 The 17β-(t-butyldimethylsilyloxy)-7α-(2-propen-1-yl)androstan-3-one (110 mg) obtained in step 1 of Example 3 was dissolved in dichloromethane (0.5 ml) and, after adding 3-benzyloxystyrene (156 mg) and benzylidenebis(tricyclohexylphosphine)-dichlororuthenium
15 (10.0 mg), the mixture was heated under reflux for 24 hours in an argon atmosphere. After standing to cool, the reaction mixture was concentrated at reduced pressure and

purified by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/3) to give the end compound in 104.1 mg (yield, 67%).

1H-NMR(300MHz, CDCl₃)δ: 7.49-7.28(5H, m), 7.21(1H, dd, J=7.9, 8.0Hz), 6.98-6.90(2H, m), 6.82(1H, dd, J=1.4, 8.0Hz), 6.30(1H, d, J=5.7Hz), 6.14-6.00(1H, m), 5.07(2H, s), 3.57(1H, dd, J=8.0, 8.5Hz), 2.46-0.92(22H, m), 1.05(3H, s), 0.88(9H, s), 0.74(3H, s), 0.01(6H, s).

Mass (EI): 626(M⁺).

10 (Step 2)



17β-(t-butyldimethylsilyloxy)-7α-[3-(3-hydroxyphenyl)propyl]-5α-androstan-3-one

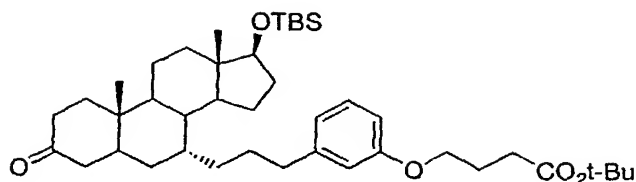
17β-(t-Butyldimethylsilyloxy)-7α-[3-(3-benzyloxy)phenyl-2-propenyl]-5α-androstan-3-one (104.1 mg) was dissolved in ethyl acetate (20 ml) and, after adding acetic acid (0.2 ml) and 10%-palladium/carbon (20 mg), the mixture was stirred for 4 hours at 25 ° in a hydrogen atmosphere. After filtering the reaction mixture, the solvent was distilled off at reduced pressure to give the end compound in 79.8 mg (yield, 89%).

1H-NMR(300MHz, CDCl₃)δ: 7.18-7.09(1H, m), 6.73(1H, d, J=7.7Hz), 6.69-6.62(2H, m), 5.07(1H, s), 3.54(1H, dd, J=8.0, 8.8Hz), 2.66-2.20(5H, m), 2.07-0.85(21H, m), 1.02(3H, s),

0.88(9H, s), 0.70(3H, s), 0.010(3H, s), 0.008(3H, s).

Mass (EI): 538(M+).

(Step 3)



5 17β-(t-butyldimethylsilyloxy)-7α-[3-(3-(3-t-butoxycarbonylpropoxy)phenyl)propyl]-5α-androstan-3-one

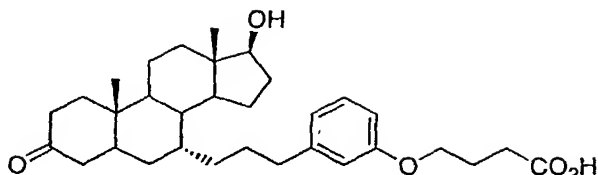
In a nitrogen atmosphere, 17β-(t-butyldimethylsilyloxy)-7α-[3-(3-hydroxyphenyl)propyl]-5α-androstan-3-one (30.2 mg), potassium carbonate (62 mg), 3-bromobutanoic acid t-butyl ester (0.020 ml) and 18-crown-6 (100 mg) were dissolved in N,N-dimethylacetamide (0.2 ml) and the solution was stirred for 10 minutes at 60°C. After adding water to the reaction mixture, extraction was effected using a solvent system consisting of a mixture of ethyl acetate and hexane. The organic layer was dried with sodium sulfate and, after filtering, the solvents were distilled off at reduced pressure. The resulting residue was purified by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 1/5) to give the end compound in 24.8 mg (yield, 80%).

¹H-NMR(300MHz, CDCl₃)δ: 7.22-7.13(1H, m), 6.79-6.67(3H, m), 3.98(2H, t, J=6.1Hz), 3.54(1H, dd, J=8.0, 8.5Hz), 2.65-2.14(5H, m), 2.43(2H, t, J=7.4Hz), 2.12-0.90(23H, m), 1.45(9H, s), 1.02(3H, s), 0.88(9H, s), 0.71(3H, s),

0.009(3H, s), 0.005(3H, s).

Mass (EI): 567(M+).

(Step 4)



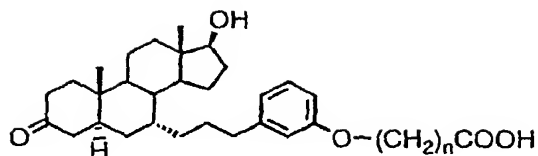
5 17β-hydroxy-7α-[3-{3-(3-carboxypropoxy)phenyl}propyl]-5α-androstan-3-one

17β-(t-Butyldimethylsilyloxy)-7α-[3-{3-(3-t-butoxycarbonylpropoxy)phenyl}propyl]-5α-androstan-3-one (24.8 mg) was dissolved in acetone (4 ml) and, after adding
 10 6 N-hydrochloric acid (1 ml), the mixture was heated under reflux for 2 hours. After distilling off the solvent at reduced pressure, purification was effected by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 2/1) to give the end compound in 19.0 mg
 15 (yield, 100%).

¹H-NMR(300MHz, CDCl₃)δ: 7.16(1H, dd, J=7.1, 8.0Hz), 6.80-6.68(3H, m), 4.02(2H, dt, J=1.4, 6.3Hz), 3.63(1H, dd, J=8.2, 8.8Hz), 3.56(1H, br), 3.13-2.98(4H, m), 2.45-1.95(8H, m), 1.82-0.94(18, m), 1.03(3H, s), 0.74(3H, s).

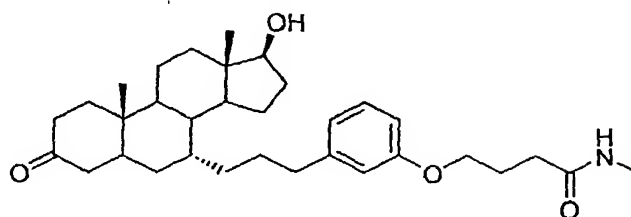
20 Mass (ESI): 511(M+1).

The following compound was synthesized by a similar method to Example 162.



Example	n	MW	Mass (FAB)
163	4	524	525

[Example 164]



5 Synthesis of 17β-hydroxy-7α-[3-[3-{3-(N-methylaminocarbonyl)propoxy}phenyl]propyl]-5α-androstan-3-one

The 17β-hydroxy-7α-[3-{3-(3-carboxypropoxy)phenyl}propyl]-5α-androstan-3-one (6.6 mg)
 10 obtained in Example 162 was dissolved in tetrahydrofuran (0.5 ml) and, after adding 1-(N,N-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (8.1 mg), 1-hydroxybenzotriazole monohydrate (6.4 mg) and methylamine 40% methanol solution (60 μl), the mixture was stirred for
 15 18 hours at 25°C. After adding ethyl acetate (2.0 ml), the reaction mixture was washed with 1 N-hydrochloric acid, 1 N aqueous solution of sodium hydroxide, and a saturated aqueous solution of sodium chloride. The organic layer was

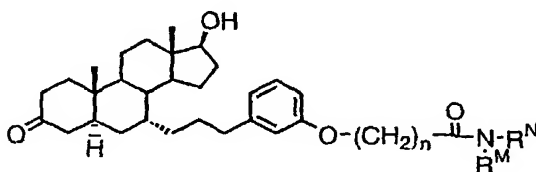
dried with magnesium sulfate and, after filtering, the solvent was distilled off at reduced pressure. The resulting residue was purified by silica gel column chromatography (developing solvents: ethyl acetate/n-hexane = 5/1) to give the end compound in 0.6 mg (yield, 8.8%).

¹H-NMR(270MHz, CDCl₃)δ: 0.75(3H, s), 1.03(3H, s), 1.05-1.95(22H, m), 1.95-2.21(5H, m), 2.26-2.42(4H, m), 2.51-2.65(2H, m), 2.81(3H, d), 3.63(1H, t, J=8.1Hz), 3.99(2H, t, J=5.9Hz), 6.70(3H, m), 7.17(1H, dd).

Mass(ESI): 524(M+1).

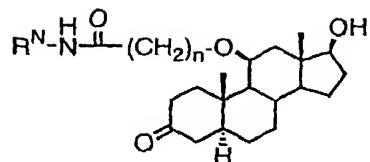
R_f value (on silica gel plate, developing solvents: ethyl acetate/n-hexane = 4/1): 0.21.

The following compounds were synthesized by similar methods to Example 164.



Example	n	R ^M	R ^N	MW	Mass(ESI)
165	4	H	Me	537	538
166	4	Me	Me	551	552
167	4	-(CH ₂) ₄ -		577	578
168	3	Me	Me	537	538
169	3	-(CH ₂) ₄ -		563	564

The following compounds were synthesized by similar methods to Example 114.



Example	n	R ^N	MW	Mass (FAB)
170	5	H	419	420
171	5	n-pentyl	489	490
172	7	H	447	548
173	7	n-pentyl	517	518
174	9	H	475	476
175	9	n-pentyl	545	546
176	11	H	503	504
177	11	n-pentyl	573	574
178	13	H	531	532
179	13	n-pentyl	601	602

[Example 180] Evaluating the agonist and antagonist actions

5 The compound of Example 4 was evaluated for its agonist and antagonist actions in relation to the androgen receptor mediated transcriptional activity.

10 The agonist action was measured by the same method as described in Example 1; the agonist activity was computed by the following formula and the determined agonist activity was used to compute the FI₅ value (the concentration for a compound treated group at which it shows a transcriptional activity five times the transcriptional activity for the case where the compound is not added). The compound was added at concentrations of 1, 15 10, 100, 1000 and 10000 nmol/L.

Agonist activity = Transcriptional activity when
the compound was added/Transcriptional activity
when the compound was not added

The antagonist action was measured by the same method
5 as described in Example 2; the antagonist activity was
computed by the following formula and the determined
antagonist activity was used to compute the IC₅₀ value (the
concentration for a compound treated group at which it
shows a 50% decrease in the transcriptional activity of DHT
10 0.1 nmol/L when the compound was not added).. The compound
was added at concentrations of 1, 10, 100, 1000 and 10000
nmol/L and at each of these concentrations, measurement was
done in the presence of DHT (0.1 nmol/L).

15 Antagonist activity = Transcriptional activity when
the compound was added/Transcriptional activity
when the compound was not added x 100

Compound	IC ₅₀ value (nM)	FI ₅ value (nM)
Compound of Example 9	451	ND*
10	937	ND
14	1984	ND
18	342	ND
19	295	ND
20	37	ND
23	1302	ND
24	477	ND
25	415	ND
26	1128	ND
27	421	ND
28	1614	ND
29	304	ND
30	733	ND

42	342	ND
43	1299	ND
46	1751	ND
50	737	ND
51	474	ND
52	277	ND
64	809	ND
65	1831	ND
73	1099	ND
74	2036	ND
96	1601	ND
164	291	ND
167	475	ND
168	540	ND
EM-101	2619	ND
Hydroxyflutamide	31	1000
Bicaltamide	136	767

* ND* in the table signifies that even when the compound was added at a concentration of 10000 nM, the transcriptional activity of the compound-treated group was less than 5 times the transcriptional activity of the control group, making it impossible to compute the FI₅ value.

The above test results verify that existing anti-androgenic agents, hydroxyflutamide and bicaltamide, also exhibit agonist action for the androgen receptor mediated transcriptional activity whereas the compounds of the invention are substantially free of such agonist action for the androgen receptor mediated transcriptional activity. Thus, it is suggested that the compounds of the invention can potentially reduce the development of androgen

tolerance which has been a problem with the conventionally used antiandrogenic agents.

It has also been verified that the compounds of the invention have better agonist action than EM-101. Thus, it is suggested that the compounds of the invention have a sufficient antiandrogenic action to be used as pharmaceuticals and that they can advantageously be used as antiandrogenic agents.

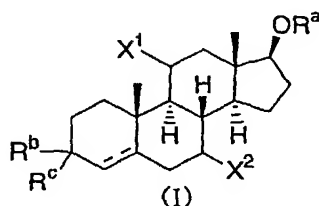
10 INDUSTRIAL APPLICABILITY

The compounds of the invention which are represented by the general formula (I) and the substances of the invention which act as antagonist against but not as agonist for the androgen receptor are potential antiandrogenic agents that do exhibit any side effects such as the development of androgen tolerance due to long-term administration and/or hepatotoxicity and, hence, are expected to be useful as pharmaceutical compositions, say, therapeutics for diseases such as prostate cancer, prostatomegaly, male pattern alopecia, sexual prematurity, acne vulgaris, seborrhea and hirsutism. If the compounds of the invention which are represented by the general formula (I) and the substances of the invention which act as antagonist against but not as agonist for the androgen receptor are preliminarily administered, the onset of diseases such as prostate cancer, prostatomegaly, male pattern alopecia, sexual prematurity, acne vulgaris, seborrhea and hirsutism can hopefully be prevented or

retarded, so they are also potential preventives of these diseases. Further, the compounds of the invention which are represented by the general formula (I) and the substances of the invention which act as antagonist against
5 but not as agonist for the androgen receptor have toxicity such as cytotoxicity sufficiently reduced that they are expected to find advantageous use as therapeutics and/or preventives of the diseases mentioned above.

SECRET

1. A compound represented by the general formula (I),
pharmaceutically acceptable salts thereof, or prodrugs of
the compound or its salts:



[wherein X¹ and X² represent independently a hydrogen atom or a group represented by the general formula (II)]

$$-\bar{A}r-\bar{A}-\bar{R}^1 \quad (\text{II})$$

R^a represents a hydrogen atom or a protective group of a hydroxyl group, R^b and R^c, when taken together with the carbon atom in 3-position to which they are bound, represent an optionally protected -(C=O)-, and the dashed line in combination with the solid line represents the formation of a single bond or a double bond;

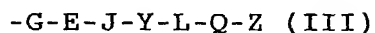
in addition, Ar represents a single bond or an aromatic hydrocarbon group, A represents a methylene group or -O-, R¹ represents an optionally substituted alkyl group, an optionally substituted alkenyl group or an optionally substituted alkynyl group;

provided that X^1 and X^2 are not a hydrogen atom at the same time].

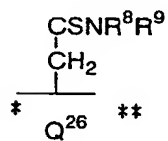
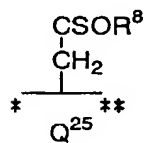
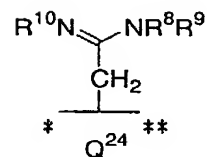
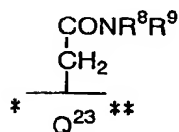
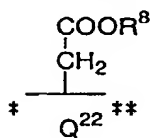
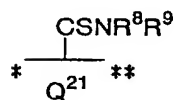
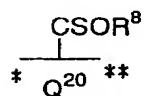
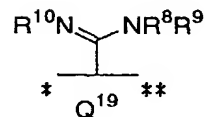
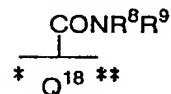
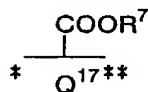
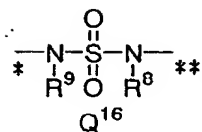
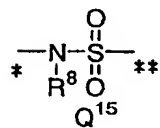
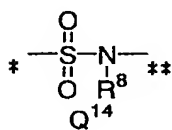
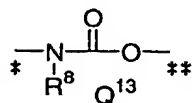
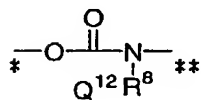
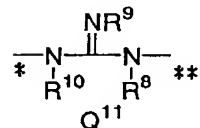
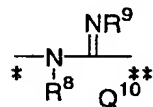
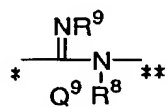
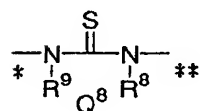
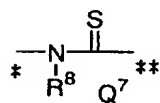
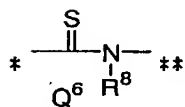
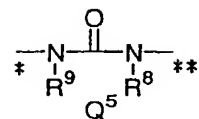
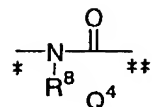
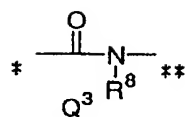
2. The compound according to claim 1, pharmaceutically

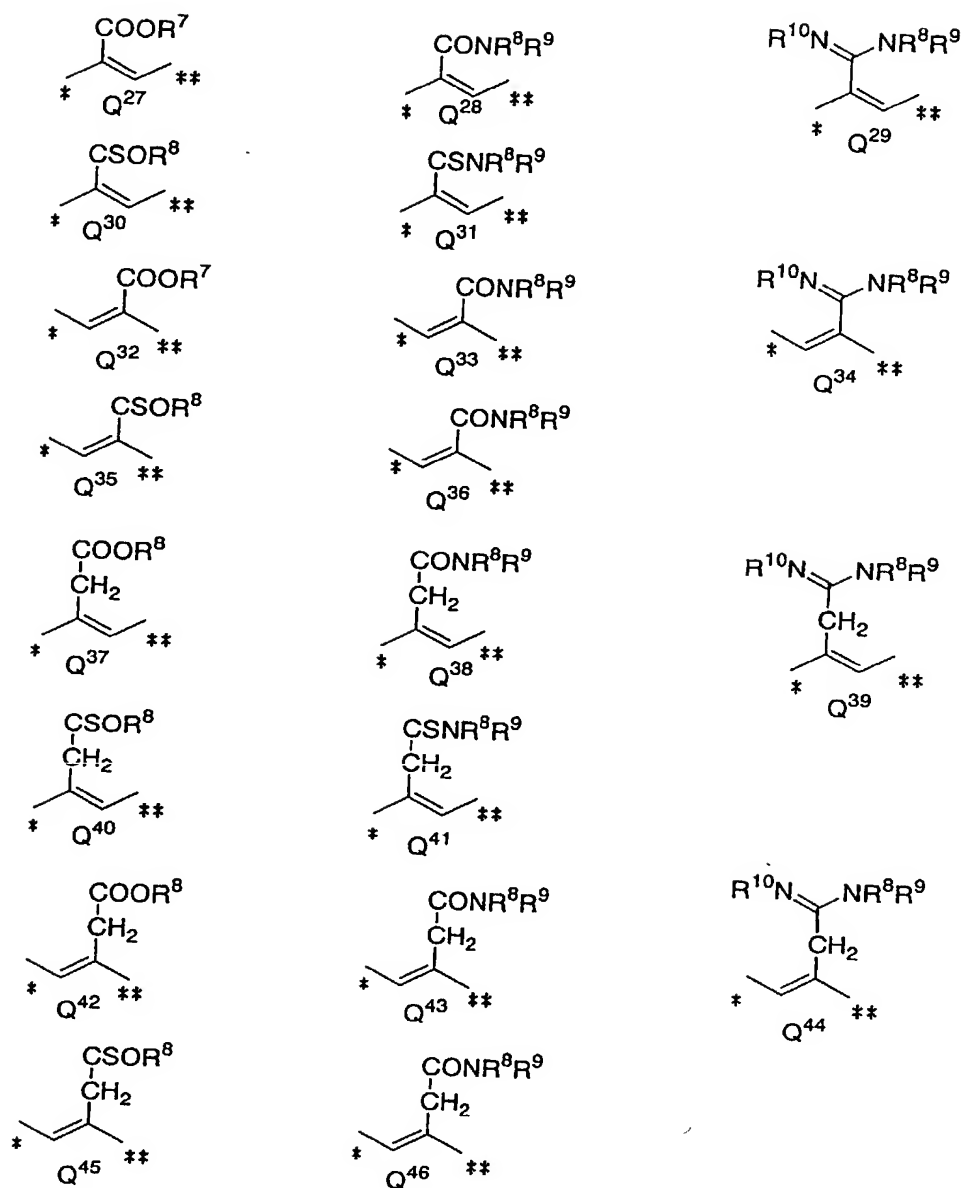
acceptable salts thereof, or prodrugs of the compound or its salts, wherein R^1 is R^{1a}

[where R^{1a} is the general formula (III)]

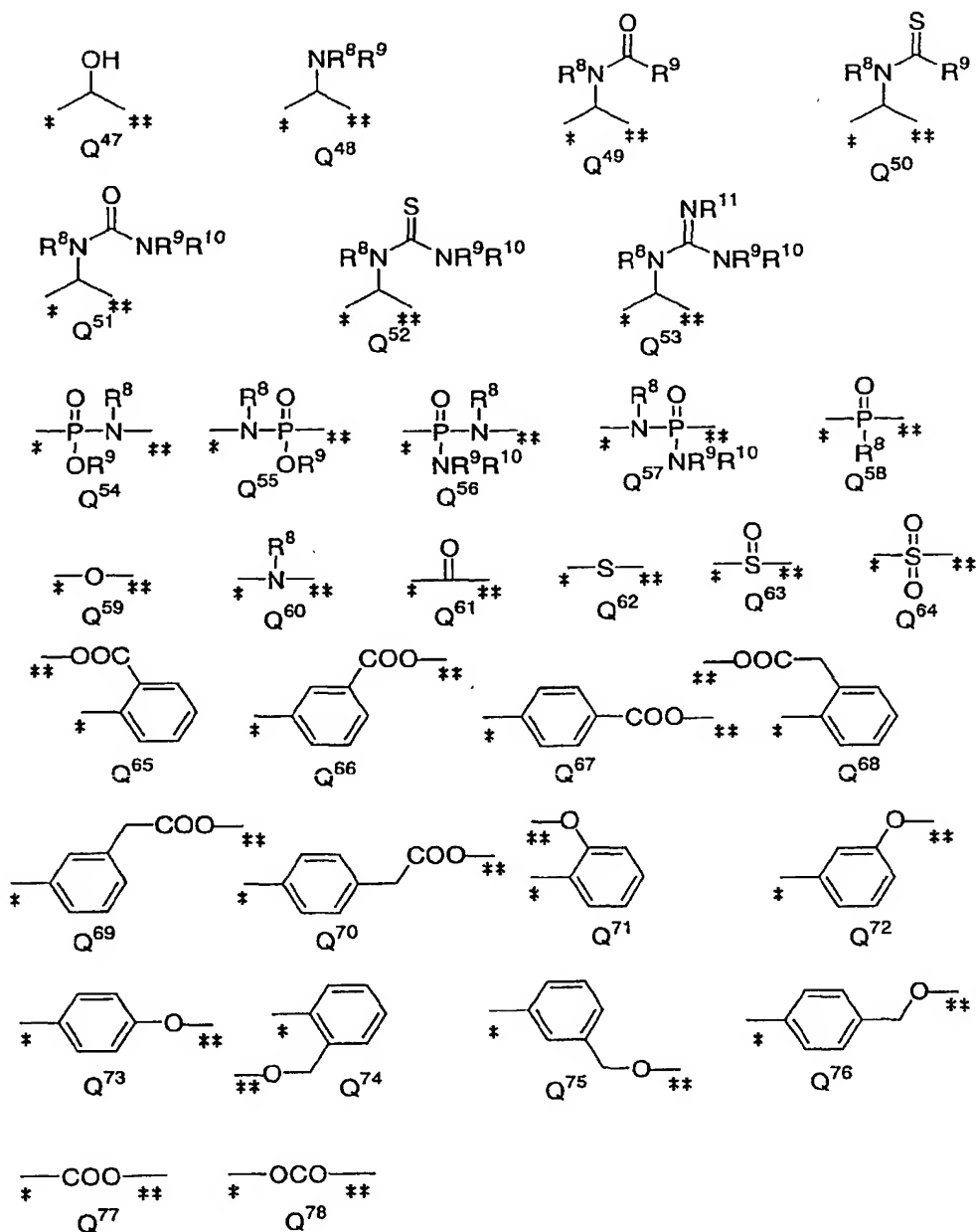


{wherein G represents an optionally substituted straight-chained or branched alkylene group having 1 - 30 carbon atoms, an optionally substituted straight-chained or branched alkenylene groups having 2 - 30 carbon atoms or an optionally substituted straight-chained or branched alkynylene group having 2 - 30 carbon atoms, E represents a single bond or -O-, J represents a single bond, an optionally substituted aromatic hydrocarbon group or an optionally substituted heterocyclic group, Y represents a single bond or -O-, L represents a single bond, a straight-chained or branched alkylene group having 1 - 10 carbon atoms, a straight-chained or branched alkenylene group having 2 - 10 carbon atoms or a straight-chained or branched alkynylene group having 2 - 10 carbon atoms, Q represents a single bond or one group selected from among the following formulae:





and



(where R^7 and R^8 represent independently a hydrogen atom or a straight-chained or branched lower alkyl group having 1 - 6 carbon atoms, R^9 , R^{10} and R^{11} each independently represent a hydrogen atom or a straight-chained or branched lower alkyl group having 1 - 3 carbon atoms), Z represents a hydrogen atom, a straight-chained or branched alkyl group

-



15. The compound according to any one of claims 1 - 13, pharmaceutically acceptable salts thereof, or prodrugs of the compound or its salts, wherein Q is Q³ where R⁸ is a hydrogen atom or Q⁴ where R⁸ is a hydrogen atom.

17. The compound according to any one of claims 1 - 11, pharmaceutically acceptable salts thereof, or prodrugs of the compound or its salts, wherein Ar is an aromatic hydrocarbon group and A is -O-.

19. The compound according to claim 18, pharmaceutically acceptable salts thereof, or prodrugs of the compound or its salts, wherein G is an optionally substituted straight-chained alkylene group having 2 - 13 carbon atoms.

- 432 -

group and a phenyl group, or $-NR^3Z^2$ may be such that N, R^8 and Z^2 combine together to form a hetero ring), $-(CH_2)_p-Ph-O-(CH_2)_q-CO-NR^8Z^3$ (Ph, p and R^8 have the same meanings as defined above, q represents an integer of at least 1, and Z^3 represents a hydrogen atom or a straight-chained or branched alkyl group having 1 - 10 carbon atoms that may optionally be substituted by any one group selected from the group consisting of a cycloalkyl group, a hydroxyl group, a carboxyl group, a heterocyclic group and a phenyl group, or

$-NR^8Z^3$ may be such that N, R^8 and Z^3 combine together to form a hetero ring) and $-(CH_2)_p-CH(COOH)-(CH_2)_3-CF_2-CF_3$ (p has the same meaning as defined above).

22. The compound or substance according to claim 1, pharmaceutically acceptable salts thereof, or prodrugs of the compound or substance or their salts, wherein X^1 is any one group selected from the group consisting of $-(CH_2)_p-COOH$ (p is an integer of at least 1), $-(CH_2)_p-CH(COOH)-(CH_2)_3-CF_2-CF_3$ (p has the same meaning as defined above), $-(CH_2)_p-CH(COOME)-(CH_2)_3-CF_2-CF_3$ (p has the same meaning as defined above), $-O-(CH_2)_p-COOH$ (p has the same meaning as defined above), $-O-(CH_2)_p-CH(COOH)-(CH_2)_3-CF_2-CF_3$ (p has the same meaning as defined above), $-(CH_2)_p-S-(CH_2)_3-CF_2-CF_3$ (p has the same meaning as defined above), $-(CH_2)_p-SO-(CH_2)_3-CF_2-CF_3$ (p has the same meaning as defined above), $-O-(CH_2)_p-SO-(CH_2)_3-CF_2-CF_3$ (p has the same meaning as defined above), $-O-(CH_2)_p-SO_2-(CH_2)_3-CF_2-CF_3$ (p has the same meaning as defined above), $-Ph-O-CH_3$ (Ph represents a phenylene group), $-Ph-O-$

(CH₂)_p-COOH (Ph and p have the same meanings as defined above), -(CH₂)_p-CO-NR⁸Z³ (p has the same meaning as defined above, R⁸ represents a hydrogen atom or a straight-chained or branched lower alkyl group having 1 - 6 carbon atoms, Z³ represents a hydrogen atom or a straight-chained or branched alkyl group having 1 - 10 carbon atoms that may optionally be substituted by any one group selected from the group consisting of a cycloalkyl group, a hydroxyl group, a carboxyl group, a heterocyclic group and a phenyl group, or -NR⁸Z³ may be such that N, R⁸ and Z³ combine together to form a hetero ring), -Ph-O-(CH₂)_p-CO-NR⁸Z³ (Ph, p, R⁸, Z³ and -NR⁸Z³ have the same meanings as defined above) and -O-(CH₂)_p-CO-NR⁸Z³ (p, R⁸, Z³ and -NR⁸Z³ have the same meanings as defined above).

23. The compound according to any one of claims 1 - 3, pharmaceutically acceptable salts thereof, or prodrugs of the compound or its salts, which is selected from among 17β-hydroxy-7α-{7-(N,N-dimethylaminocarbonyl)heptyl}-5α-androstan-3-one;

17β-hydroxy-7α-{7-(N-ethylaminocarbonyl)heptyl}-5α-androstan-3-one;

17β-hydroxy-7α-[7-(N-(isopropylaminocarbonyl)heptyl)]-5α-androstan-3-one;

17β-hydroxy-7α-[7-(N-methyl-N-butylaminocarbonyl)heptyl]-5α-androstan-3-one;

17β-hydroxy-7α-[7-(N,N-diethylaminocarbonyl)heptyl]-5α-androstan-3-one;

17β-hydroxy-7α-[7-(piperidinocarbonyl)heptyl]-5α-androstan-

$\frac{1}{\sqrt{2}} \begin{pmatrix} 1 & i \\ 0 & 1 \end{pmatrix}$

17 β -hydroxy-7 α -[7-{7-(N-methylaminocarbonyl)heptyl}-5 α -androstan-3-one;

17 β -hydroxy-7 α -[7-(N-methyl-N-propylaminocarbonyl)heptyl]-
5 α -androstane-3-one;

17 β -hydroxy-7 α -[7-(N-methyl-N-benzylaminocarbonyl)heptyl]-
5 α -androstane-3-one;

17 β -hydroxy-7 α -[7-(1-pyrrolidinylcarbonyl)heptyl]-5 α -
androstan-3-one;

17 β -hydroxy-7 α -[7-(morpholinocarbonyl)heptyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[9-(N,N-dimethylaminocarbonyl)nonyl]-5 α -androstan-3-one:

17 β -hydroxy-7 α -[9-(N,N-diethylaminocarbonyl)nonyl]-5 α -androstane-3-one;

17 β -hydroxy-7 α -[9-(N-methyl-N-butylaminocarbonyl)nonyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[9-(N-methyl-N-propylaminocarbonyl)nonyl]-
5 α -androstan-3-one;

17 β -hydroxy-7 α -[9-(morpholinocarbonyl)nonyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[10-(N,N-dimethylaminocarbonyl)decyl]-5 α -

androstan-3-one;

17 β -hydroxy-7 α -[7-{N-(2-hydroxyethyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[7-(N-propylaminocarbonyl)heptyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[7-(N-benzylaminocarbonyl)heptyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[7-{N-(2-phenylethyl)aminocarbonyl}heptyl]-5 α -androstan-3-one;

17 β -hydroxy-11 β -[9-(N,N-diethylaminocarbonyl)nonyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[3-[3-{3-(N-methylaminocarbonyl)propoxy}phenyl]propyl]-5 α -androstan-3-one;

17 β -hydroxy-7 α -[3-[3-{3-(N,N-dimethylaminocarbonyl)propoxy}phenyl]propyl]-5 α -androstan-3-one; and

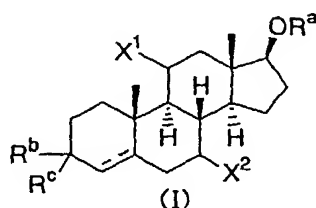
17 β -hydroxy-7 α -[3-[3-{4-(1-pyrrolidinylcarbonyl)butoxy}phenyl]propyl]-5 α -androstan-3-one.

24. A substance which acts as antagnoist against but not as agonist for the androgen receptor, or pharmaceutically acceptable salts thereof, or prodrugs of the substance or its salts.

25. A pharmaceutical composition containing as an active ingredient the compound or substance according to any one of claims 1 - 24, or pharmaceutically acceptable salts thereof, or prodrugs of the compound or substance or their

ABSTRACT

Compounds represented by the general formula (I),
pharmaceutically acceptable salts thereof, or prodrugs of
5 the compounds or their salts:



[wherein X^1 and X^2 represent independently a hydrogen atom,
10 or a group represented by the general formula (II)
 $-\text{Ar}-\text{A}-\text{R}^1$ (II)]

R^a represents a hydrogen atom or a protective group of a
hydroxyl group, R^b and R^c , when taken together with the
carbon atom in 3-position to which they are bound,
15 represent an optionally protected $-(\text{C}=\text{O})-$, and the dashed
line in combination with the solid line represents the
formation of a single bond or a double bond;

in addition, Ar represents a single bond or an
aromatic hydrocarbon group, A represents a methylene group
20 or $-\text{O}-$, R^1 represents an optionally substituted alkyl group,
an optionally substituted alkenyl group or an optionally
substituted alkynyl group;

provided that X^1 and X^2 are not a hydrogen atom at the
same time], as well as substances that act as antagonist
25 against but not as agonist for the androgen receptor,

pharmaceutically acceptable salts thereof, or prodrugs of
the substances or their salts are useful as antiandrogenic
agents and may be used as preventives or therapeutics of a
disease selected from prostate cancer, prostatomegaly, male
5 pattern alopecia, sexual prematurity, acne vulgaris,
seborrhea and hirsutism.

Combined Declaration for Patent Application and Power of Attorney

As a below-named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name; and that I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

ANTIANDROGENIC AGENTS

the specification of which (check one)

☐ is attached hereto;

☐ was filed in the United States under 35 U.S.C. §111 on _____, as U.S. Appln. No. _____*; or

☒ was/will be filed in the U.S. under 35 U.S.C. §371 by entry into the U.S. national stage of an international (PCT) application, PCT/JP00/05636 filed Aug. 23, 2000, entry requested on _____*; national stage application received U.S. Appln. No. _____*; §371/§102(e) date _____* (* if known)

and was amended on _____ (if applicable).

(include dates of amendments under PCT Art. 19 and 34 if PCT)

I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above; and I acknowledge the duty to disclose to the Patent and Trademark Office (PTO) all information known by me to be material to patentability as defined in 37 C.F.R. §1.56.

I hereby claim foreign priority benefits under 35 U.S.C. §§ 119 and 365 of any prior foreign application(s) for patent or inventor's certificate, or prior PCT application(s) designating a country other than the U.S., listed below with the "Yes" box checked and have also identified below any such application having a filing date before that of the application on which priority is claimed:

274956/1999	Japan	23/8/1999	<input checked="" type="checkbox"/>	<input type="checkbox"/>
(Number)	(Country)	(Day Month Year Filed)	YES	NO
338334/1999	Japan	22/10/1999	<input checked="" type="checkbox"/>	<input type="checkbox"/>
(Number)	(Country)	(Day Month Year Filed)	YES	NO
237721/2000	Japan	30/6/2000	<input checked="" type="checkbox"/>	<input type="checkbox"/>
(Number)	(Country)	(Day Month Year Filed)	YES	NO
219800/2000	Japan	19/7/2000	<input checked="" type="checkbox"/>	<input type="checkbox"/>
(Number)	(Country)	(Day Month Year Filed)	YES	NO

I hereby claim the benefit under 35 U.S.C. §120 of any prior U.S. non-provisional application(s) or prior PCT application(s) designating the U.S. listed below, or under §119(e) of any prior U.S. provisional applications listed below, and, insofar as the subject matter of each of the claims of this application is not disclosed in such U.S. or PCT application in the manner provided by the first paragraph of 35 U.S.C. §112, I acknowledge the duty to disclose to the PTO all information as defined in 37 C.F.R. §1.56(a) which occurred between the filing date of the prior application and the national filing date of this application:

_____ (Application No.)	_____ (Day Month Year Filed)	_____ (Status: patented, pending, abandoned)
_____ (Application No.)	_____ (Day Month Year Filed)	_____ (Status: patented, pending, abandoned)
_____ (Application No.)	_____ (Day Month Year Filed)	_____ (Status: patented, pending, abandoned)

As a named inventor, I hereby appoint the following registered practioners to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

All of the practioners associated with Customer Number 001444

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The undersigned hereby authorizes the U.S. Attorneys or Agents appointed herein to accept and follow instructions from _____ as to any action to be taken in the U.S. Patent and Trademark Office regarding this application without direct communication between the U.S. Attorneys or Agents and the undersigned. In the event of a change of the persons from whom instructions may be taken, the U.S. Attorneys or Agents appointed herein will be so notified by the undersigned.

Page 2 of 2 Pages

Title: ANTIANDROGENIC AGENTS

Atty. Docket:

U.S. Application filed

Serial No.

PCT Application filed

August 23, 2000

Serial No.

PCT/JP00/05636

I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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POST OFFICE ADDRESS			

ALL INVENTORS MUST REVIEW APPLICATION AND DECLARATION BEFORE SIGNING. ALL ALTERATIONS MUST BE INITIALED AND DATED BY ALL INVENTORS PRIOR TO EXECUTION. NO ALTERATIONS CAN BE MADE AFTER THE DECLARATION IS SIGNED. ALL PAGES OF DECLARATION MUST BE SEEN BY ALL INVENTORS.